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 NEWS 23  JUL 28  EPFULL enhanced with additional legal status
                  information from the epoline Register
 NEWS 24  JUL 28  IFICDB, IFIPAT, and IFIUDB reloaded with
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 NEWS 25  JUL 28  STN Viewer performance improved
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=> s hey1 or hey 1
L1          299 HEY1 OR HEY 1

=> s l1 and (bone or osteo?)
L2           83 L1 AND (BONE OR OSTEO?)
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=> dup rem l2
PROCESSING COMPLETED FOR L2
L3            58 DUP REM L2 (25 DUPLICATES REMOVED)

=> d bib abs 1-
YOU HAVE REQUESTED DATA FROM 58 ANSWERS - CONTINUE? Y/(N):y

L3   ANSWER 1 OF 58  CAPLUS  COPYRIGHT 2008 ACS on STN
AN   2008:858029  CAPLUS
DN   149:145062
TI   Mir-16 regulated genes and pathways as targets for therapeutic
     intervention
IN   Byrom, Mike; Patrawala, Lubna; Johnson, Charles D.; Brown,
David; Bader,
     Andreas G.
PA   Asuragen, Inc., USA
SO   PCT Int. Appl., 183pp.
     CODEN: PIXXD2
DT   Patent
LA   English
FAN.CNT 7
     PATENT NO.          KIND   DATE        APPLICATION NO.
DATE
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PI   WO 2008085797        A2    20080717    WO 2007-US89206
20071231
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EG, ES,
             FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS,
JP, KE,
             KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY,
MA, MD,
             ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM,
PG, PH,
             PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY,
TJ, TM,
             TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
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HU, IE,
             IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK,
TR, BF,
             BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD,
TG, BW,
             GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW,
AM, AZ,
             BY, KG, KZ, MD, RU, TJ, TM
     WO 2008073923        A2    20080619    WO 2007-US87038
20071210
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY,
BZ, CA,
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GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG,
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MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL,
PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN,
TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF,
BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW,
GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ,
BY, KG, KZ, MD, RU, TJ, TM
PRAI US 2006-869295P P 20061208
US 2006-882758P P 20061229
WO 2007-US87038 A 20071210

AB The present invention concerns methods and compns. for identifying genes or genetic pathways modulated by miR-16, using miR-16 to modulate a gene or gene pathway, using this profile in assessing the condition of a patient and/or treating the patient with an appropriate miRNA. Thus, a gene expression profile of A549 cells transfected with hsa-miR-16 was determined This miRNA primarily affected pathways related to cellular growth, development, and proliferation. Since these processes all have integral roles in the development and progression of various cancers manipulation of the expression of genes involved in these pathways represents a potentially useful therapy for cancer.

L3 ANSWER 2 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2008:796722 CAPLUS
DN 149:120555
TI Novel methods for functional analysis of high-throughput experimental data and gene groups for breast tumor
IN Nikolsky, Yuri; Bugrim, Andrej; Nikolskaya, Tatiana
PA USA
SO PCT Int. Appl., 84pp.

CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2008079269	A2	20080703	WO 2007-US26014	20071219

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRAI US 2006-875648P P 20061219

AB The present invention relates generally to groups of genes that can be used to diagnose and differentiate between types of specific diseases such as breast cancer. The groups of genes can be further used to develop diagnostic kits for the specific diseases. The diagnostic kits can also differentiate between sub-categories of a disease to help identify the appropriate treatment regimen for a patient.

L3 ANSWER 3 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2008:703414 CAPLUS
DN 149:49493
TI Stem/progenitor cell-specific microRNAs and their regulated gene complement and diagnostic and therapeutic applications
IN Georgantas, Robert; Civin, Curt I.; Calin, George Adrian; Croce, Carlo

Maria
PA The Johns Hopkins University, USA; Ohio State University
SO PCT Int. Appl., 434pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2008070082	A2	20080612	WO 2007-US24845	20071204

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRAI US 2006-872764P P 20061204

AB Thirty-three microRNAs are discovered to be expressed in CD34+ hematopoietic stem-progenitor cells (HSPCs) from normal human bone marrow and mobilized human peripheral blood stem cell harvests. The inventors bioinformatically combined (1) human microRNA expression data, (2) mRNA expression data obtained for human CD34+ cells from a previous study by the inventors, and (3) the predicted mRNA targets of all known microRNAs. Combining these data sets into one database enabled the insilico examination of the interactions between HSPC-expressed microRNAs (HE-miRNAs) and mRNAs. Based on bairing HE-miRNAs with their putative

HSPC-expressed mRNA targets, along with annotation implicating certain of these targets as associated with hematopoietic differention, it is possible to predict which HE-miRNAs control hematopoietic differentiation. MicroRNA cotrol of several of the target mRNAs was validated by demonstrating that their translation in fact is decreased by microRNAs. MicroRNA-155 was chosen for functional characterization in hematopoiesis, because it was predicted that it would control both myelopoiesis and erythropoiesis, and as predicted, microRNA-155 transduction greatly reduced both myeloid and erythroid colony formation of normal human HSPCs. Thus, methods and compns. are provided for modulating the differentiation of incompletely differentiated cells, such as stem-progenitor cells, e.g., hematopoietic stem-progenitor cells.

L3 ANSWER 4 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2008:320290 CAPLUS
DN 148:328847
TI Gene expression profiling in the diagnosis, classification, and staging of melanoma
IN Riker, Adam I.; Enkemann, Steven Alan
PA H. Lee Moffitt Cancer Center and Research Institute, Inc., USA; University of South Florida
SO PCT Int. Appl., 89pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2008031041	A2	20080313	WO 2007-US77895	20070907

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL,

PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN,
TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF,
BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW,
GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ,
BY, KG, KZ, MD, RU, TJ, TM
US 20080113360 A1 20080515 US 2007-852102 20070907
PRAI US 2006-824849P P 20060907
WO 2007-US77895 A 20070907
AB Marker genes that show changes in levels of expression in melanoma
compared to normal epithelial melanocytes and that can be used to diagnose
different forms of melanoma are identified. These markers can also be
used to distinguish primary and metastatic melanomas. Possible oncogenes
for melanoma are also identified.

L3 ANSWER 5 OF 58 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
DUPLICATE 1
AN 2008:429476 BIOSIS
DN PREV200800429475
TI Zfp64 participates in Notch signaling and regulates differentiation in
mesenchymal cells.
AU Sakamoto, Kei [Reprint Author]; Tamamura, Yoshihiro; Katsube, Ken-ichi;
Yamaguchi, Akira
CS Tokyo Med and Dent Univ, Grad Sch, Sect Oral Pathol, Bunkyo Ku, 1-5-45
Yushima, Tokyo 1138549, Japan
s-kei.mpa@tmd.ac.jp
SO Journal of Cell Science, (MAY 15 2008) Vol. 121, No. 10, pp. 1613-1623.
CODEN: JNCSAI. ISSN: 0021-9533.
DT Article
LA English
ED Entered STN: 6 Aug 2008
Last Updated on STN: 6 Aug 2008
AB Notch signaling is required for multiple aspects of tissue and cell
differentiation. In this study, we identified zinc finger protein 64

(Zfp64) as a novel coactivator of Notch1. Zfp64 is associated with the intracellular domain of Notch1, recruited to the promoters of the Notch target genes Hes1 and Hey1, and transactivates them. Zfp64 expression is under the control of Runx2, and is upregulated by direct transactivation of its promoter. Zfp64 suppresses the myogenic differentiation of C2C12 cells and promotes their osteoblastic differentiation. Our data demonstrate two functions of Zfp64: (1) it is a downstream target of Runx2 and, (2) its cognate protein acts as a coactivator of Notch1, which suggests that Zfp64 mediates mesenchymal cell differentiation by modulating Notch signaling.

L3 ANSWER 6 OF 58 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
DUPLICATE 2
AN 2008:287630 BIOSIS
DN PREV200800290363
TI Notch signaling through jagged-1 is necessary to initiate chondrogenesis in human bone marrow stromal cells but must be switched off to complete chondrogenesis.
AU Oldershaw, Rachel A.; Tew, Simon R.; Russell, Amanda M.; Meade, Kate; Hawkins, Robert; McKay, Tristan R.; Brennan, Keith R.; Hardingham, Timothy E. [Reprint Author]
CS Univ Manchester, Fac Life Sci, UK Ctr Tissue Engn, Oxford Rd, Manchester M13 9PT, Lancs, UK
timothy.e.hardingham@manchester.ac.uk
SO Stem Cells (Miamisburg), (2008) Vol. 26, No. 3, pp. 666-674. ISSN: 1066-5099.
DT Article
LA English
ED Entered STN: 23 Apr 2008
Last Updated on STN: 23 Apr 2008
AB We investigated Notch signaling during chondrogenesis in human bone marrow stromal cells (hMSC) in three-dimensional cell aggregate culture. Expression analysis of Notch pathway genes in 14-day chondrogenic cultures showed that the Notch ligand Jagged-1 (Jag-1) sharply increased in expression, peaking at day 2, and then declined. A Notch target gene, HEY-1, was also expressed, with a temporal profile that closely followed the expression of Jag-1, and this preceded the rise in type II collagen expression that characterized

chondrogenesis. We demonstrated that the shut-down in Notch signaling was critical for full chondrogenesis, as adenoviral human Jag-1 transduction of hMSC, which caused continuous elevated expression of Jag-1 and sustained Notch signaling over 14 days, completely blocked chondrogenesis. In these cultures, there was inhibited production of extracellular matrix, and the gene expression of aggrecan and type II collagen were strongly suppressed; this may reflect the retention of a prechondrogenic state. The JAG-1-mediated Notch signaling was also shown to be necessary for chondrogenesis, as N-[N-(3,5-difluorophenacetyl-L-alanyl)]-(S)-phenylglycine t-butyl ester (DAPT) added to cultures on days 0-14 or just days 0-5 inhibited chondrogenesis, but DAPT added from day 5 did not. The results thus showed that Jag-1-mediated Notch signaling in hMSC was necessary to initiate chondrogenesis, but it must be switched off for chondrogenesis to proceed.

L3 ANSWER 7 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2008:282150 CAPLUS
DN 148:445573
TI BMP signaling in dermal papilla cells is required for their hair follicle-inductive properties
AU Rendl, Michael; Polak, Lisa; Fuchs, Elaine
CS Howard Hughes Medical Institute, Laboratory of Mammalian Cell Biology and Development, The Rockefeller University, New York, NY, 10021, USA
SO Genes & Development (2008), 22(4), 543-557
CODEN: GEDEEP; ISSN: 0890-9369
PB Cold Spring Harbor Laboratory Press
DT Journal
LA English
AB Hair follicle (HF) formation is initiated when epithelial stem cells receive cues from specialized mesenchymal dermal papilla (DP) cells. In culture, DP cells lose their HF-inducing properties, but during hair growth in vivo, they reside within the HF bulb and instruct surrounding epithelial progenitors to orchestrate the complex hair differentiation program. To gain insights into the mol. program that maintains DP cell

fate, we previously purified DP cells and four neighboring populations and defined their cell-type-specific mol. signatures. Here, we exploit this information to show that the bulb microenvironment is rich in bone morphogenetic proteins (BMPs) that act on DP cells to maintain key signature features in vitro and hair-inducing activity in vivo. By employing a novel in vitro/in vivo hybrid knockout assay, we ablate BMP receptor 1a in purified DP cells. When DPs cannot receive BMP signals, they lose signature characteristics in vitro and fail to generate HFs when engrafted with epithelial stem cells in vivo. These results reveal that BMP signaling, in addition to its key role in epithelial stem cell maintenance and progenitor cell differentiation, is essential for DP cell function, and suggest that it is a critical feature of the complex epithelial-mesenchymal cross-talk necessary to make hair.
RE.CNT 62 THERE ARE 62 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 8 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2008:405942 CAPLUS
DN 148:493184
TI Lamin A-dependent misregulation of adult stem cells associated with accelerated ageing
AU Scaffidi, Paola; Misteli, Tom
CS National Cancer Institute, NIH, Bethesda, MD, 20892, USA
SO Nature Cell Biology (2008), 10(4), 452-459
CODEN: NCBIFN; ISSN: 1465-7392
PB Nature Publishing Group
DT Journal
LA English
AB The premature-aging disease Hutchinson-Gilford Progeria Syndrome (HGPS) is caused by constitutive production of progerin, a mutant form of the nuclear architectural protein lamin A. Progerin is also expressed sporadically in wild-type cells and has been linked to physiol. aging. Cells from HGPS patients exhibit extensive nuclear defects, including abnormal chromatin structure and increased DNA damage. At the organismal level, HGPS affects

several tissues, particularly those of mesenchymal origin. How the cellular defects of HGPS cells lead to the organismal defects has been unclear. Here, we provide evidence that progerin interferes with the function of human mesenchymal stem cells (hMSCs). We find that expression of progerin activates major downstream effectors of the Notch signaling pathway. Induction of progerin in hMSCs changes their mol. identity and differentiation potential. Our results support a model in which accelerated aging in HGPS patients, and possibly also physiol. aging, is the result of adult stem cell dysfunction and progressive deterioration of tissue functions.
RE.CNT 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 9 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2007:113586 CAPLUS
DN 146:226597
TI Gene expression profiles in esophageal cancer and their use in diagnosis, prognosis, therapy and drug design and selection
IN Nakamura, Yusuke; Daigo, Yataro; Nakatsuru, Shuichi
PA Oncotherapy Science, Inc., Japan; The University of Tokyo
SO PCT Int. Appl., 249pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007013671	A2	20070201	WO 2006-JP315342	20060726
WO 2007013671	A3	20070830		

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US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ,
CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH,
GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA
EP 1907582 A2 20080409 EP 2006-782211 20060726
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR
PRAI US 2005-703263P P 20050727
WO 2006-JP315342 W 20060726
AB In order to identify the mols. involved in esophageal carcinogenesis and
those to be useful for diagnostic markers as well as targets for new drugs
and immunotherapy, a cDNA microarray representing 32,256 genes was
constructed to analyze the expression profiles of 19 esophageal
squamous-cell carcinomas (ESCCS) purified by laser-capture
microdissection. A detailed genome-wide database for sets of genes that
are significantly up- or down-regulated in esophageal cancer is disclosed
herein. These genes find use in the development of therapeutic drugs or
immunotherapy as well as tumor markers. Addnl., genes associated with
lymph-node metastasis and post-surgery recurrence are disclosed herein.
Among the candidate mol. target genes, a Homo sapiens epithelial cell
transforming sequence 2 oncogene (ECT2) and a cell division cycle 45, S.
cerevisiae, homolog-like (CDC45L) are further characterized. Treatment of
ESCC cells with small interfering RNAs (siRNAs) of ECT2 or CDC45L
suppressed growth of the cancer cells. Thus, the data herein provide
valuable information for identifying diagnostic systems and therapeutic
target mols. for esophageal cancer. Furthermore, the present inventors
have identified DKK1 as a potential biomarker for diagnosis of cancer such
as lung and esophageal cancers as well as prediction of the poor prognosis

of the patients with these diseases. DKK1 was specifically over-expressed in most lung and esophageal cancer tissues the present inventors examined, and was elevated in the sera of a large proportion of patients with these tumors. DKK1, combined with other tumor markers, could significantly improve the sensitivity of cancer diagnosis. Moreover, this mol. is also a likely candidate for development of therapeutic approaches such as antibody therapy.

L3 ANSWER 10 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2007:677809 CAPLUS
DN 147:337042
TI EGO, a novel, noncoding RNA gene, regulates eosinophil granule protein transcript expression
AU Wagner, Lori A.; Christensen, Clarissa J.; Dunn, Diane M.; Spangrude, Gerald J.; Georgelas, Ann; Kelley, Linda; Esplin, M. Sean; Weiss, Robert B.; Gleich, Gerald J.
CS School of Medicine, Department of Dermatology, University of Utah, Salt Lake City, USA
SO Blood (2007), 109(12), 5191-5198
CODEN: BLOOAW; ISSN: 0006-4971
PB American Society of Hematology
DT Journal
LA English
AB Gene expression profiling of early eosinophil development shows increased transcript levels of proinflammatory cytokines, chemokines, transcription factors, and a novel gene, EGO (eosinophil granule ontogeny). EGO is nested within an intron of the inositol triphosphate receptor type 1 (ITPR1) gene and is conserved at the nucleotide level; however, the largest open reading frame (ORF) is 86 amino acids. Sucrose d. gradients show that EGO is not associated with ribosomes and therefore is a noncoding RNA (ncRNA). EGO transcript levels rapidly increase following interleukin-5 (IL-5) stimulation of CD34+ hematopoietic progenitors. EGO RNA also is highly expressed in human bone marrow and in mature eosinophils. RNA silencing of EGO results in decreased major basic

protein (MBP) and eosinophil derived neurotoxin (EDN) mRNA expression in
developing CD34+ hematopoietic progenitors in vitro and in a CD34+ cell
line model. Therefore, EGO is a novel ncRNA gene expressed during
eosinophil development and is necessary for normal MBP and EDN transcript
expression.
RE.CNT 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 11 OF 58 EMBASE COPYRIGHT (c) 2008 Elsevier B.V. All rights
reserved on STN
AN 2007399390 EMBASE
TI Delta-Notch-and then? Protein interactions and proposed modes of
repression by Hes and Hey bHLH factors.
AU Fischer, Andreas; Gessler, Manfred (correspondence)
CS Biocenter, Theodor-Boveri-Institute, University of Wurzburg, Am Hubland,
D-97074 Wurzburg, Germany. gessler@biozentrum.uni-wuerzburg.de
SO Nucleic Acids Research, (Jul 2007) Vol. 35, No. 14, pp. 4583-4596.
Refs: 161
ISSN: 0305-1048 E-ISSN: 1362-4962 CODEN: NARHAD
CY United Kingdom
DT Journal; General Review; (Review)
FS 022 Human Genetics
029 Clinical and Experimental Biochemistry
LA English
SL English
ED Entered STN: 15 Oct 2007
Last Updated on STN: 15 Oct 2007
AB Hes and Hey genes are the mammalian counterparts of the Hairy and
Enhancer-of-split type of genes in Drosophila and they represent the
primary targets of the Delta-Notch signaling pathway. Hairy-related
factors control multiple steps of embryonic development and misregulation
is associated with various defects. Hes and Hey genes (also called Hesr,
Chf, Hrt, Herp or gridlock) encode transcriptional regulators of the basic
helix-loop-helix class that mainly act as repressors. The molecular
details of how Hes and Hey proteins control transcription are still poorly
understood, however. Proposed modes of action include direct binding to
N- or E-box DNA sequences of target promoters as well as indirect binding

through other sequence-specific transcription factors or sequestration of transcriptional activators. Repression may rely on recruitment of corepressors and induction of histone modifications, or even interference with the general transcriptional machinery. All of these models require extensive protein-protein interactions. Here we review data published on protein-protein and protein-DNA interactions of Hairy-related factors and discuss their implications for transcriptional regulation. In addition, we summarize recent progress on the identification of potential target genes and the analysis of mouse models. .COPYRGT. 2007 The Author(s).

L3 ANSWER 12 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2008:79471 CAPLUS
DN 148:175519
TI Soluble Jagged1 attenuates lateral inhibition, allowing for the clonal expansion of neural crest stem cells
AU Nikopoulos, George N.; Duarte, Maria; Kubu, Chris J.; Bellum, Stephen; Friessel, Robert; Maciag, Thomas; Prudovsky, Igor; Verdi, Joseph M.
CS Interdisciplinary Program in Molecular Genetics and Cell Biology, University of Maine, Orono, ME, USA
SO Stem Cells (Durham, NC, United States) (2007), 25(12), 3133-3142
CODEN: STCEEJ; ISSN: 1066-5099
PB AlphaMed Press
DT Journal
LA English
AB The activation of Notch signaling in neural crest stem cells (NCSCs) results in the rapid loss of neurogenic potential and differentiation into glia. We now show that the attenuation of endogenous Notch signaling within expanding NCSC clones by the Notch ligand soluble Jagged1 (sJ1), maintains NCSCs in a clonal self-renewing state in vitro without affecting their sensitivity to instructive differentiation signals observed previously during NCSC self-renewal. SJ1 functions as a competitive inhibitor of Notch signaling to modulate endogenous cell-cell communication to levels

sufficient to inhibit neural differentiation but insufficient to instruct gliogenic differentiation. Attenuated Notch signaling promotes the induction and nonclassic release of fibroblast growth factor 1 (FGF1). The functions of sJ1 and FGF1 signaling are complementary, as abrogation of FGF signaling diminishes the ability of sJ1 to promote NCSC expansion, yet the secondary NCSCs maintain the dosage sensitivity of the founder. These results validate and build upon previous studies on the role of Notch signaling in stem cell self-renewal and suggest that the differentiation bias or self-renewal potential of NCSCs is intrinsically linked to the level of endogenous Notch signaling. This should provide a unique opportunity for the expansion of NCSCs ex vivo without altering their differentiation bias for clin. cell replacement or transplant strategies in tissue repair.
RE.CNT 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 13 OF 58 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on
STN DUPLICATE 3
AN 2007:592800 BIOSIS
DN PREV200700588033
TI Inhibitory effects and target genes of bone morphogenetic protein 6 in Jurkat TAg cells.
AU Sivertsen, Einar A.; Huse, Kanutte; Hystad, Marit E.; Kersten, Christian; Smeland, Erlend B.; Myklebust, June H. [Reprint Author]
CS Radiumhosp Med Ctr, Rikshosp, Inst Canc Res, Dept Immunol, N-0310 Oslo, Norway
unehm@rr-research.no
SO European Journal of Immunology, (OCT 2007) Vol. 37, No. 10, pp. 2937-2948.
CODEN: EJIMAF. ISSN: 0014-2980.
DT Article
LA English
ED Entered STN: 21 Nov 2007
Last Updated on STN: 21 Nov 2007
AB Bone morphogenetic proteins (BMP) are multifunctional cytokines that belong to the TGF-beta superfamily. BMP have been shown to regulate haematopoietic stem cells, B lymphopoiesis and early thymocyte

differentiation. In the present study we explored the role of BMP-6 in Jurkat TAg cells. BMP-6 rapidly induced phosphorylation of Smad1/5/8, p38 and ERK1/2, followed by a potent up-regulation of ID1, ID2 and ID3. ID I and ID3 were also induced at the protein level. Genome-wide expression profiling of cells treated with BMP-6 compared to medium confirmed that ID1-ID3 were target genes of BMP-6 together with Noggin and Smad6. Furthermore, several genes involved in transcriptional regulation were also identified, including NFKBIA, HEY1, DLX2, KLF10 and early growth response 1. Stimulation with BMP-6 exerted an antiproliferative effect that was counteracted by inhibitor of DNA binding (Id) 1 siRNA, indicating that Id1 is an important downstream mediator in Jurkat TAg cells. A subset of CD4(+) T cells were found to express the BMP receptors Alk-2 and Alk-3 (type 1), in addition to BMPRII (type II). BMP-6 also induced phosphorylation of Smad1/5/8, followed by transcriptional increase in ID1-ID3 mRNA expression. However, we did not observe significant changes in Id protein expression in CD4+ T cells. Altogether, the data indicate a role for BMP-6 in human T lineage cells.

L3 ANSWER 14 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2007:1009378 CAPLUS
DN 148:259279
TI Modeling Notch signaling in normal and neoplastic hematopoiesis: global gene expression profiling in response to activated Notch expression
AU Ganapati, Uma; Tan, Hongying Tina; Lynch, Maureen; Dolezal, Milana; de Vos, Sven; Gasson, Judith C.
CS Division of Hematology-Oncology, Department of Medicine, University of California Los Angeles, Los Angeles, CA, USA
SO Stem Cells (Durham, NC, United States) (2007), 25(8), 1872-1880 CODEN: STCEEJ; ISSN: 1066-5099
PB AlphaMed Press
DT Journal
LA English
AB In normal hematopoiesis, proliferation is tightly linked to

differentiation in ways that involve cell-cell interaction with stromal elements in the bone marrow stem cell niche. Numerous in vitro and in vivo studies strongly support a role for Notch signaling in the regulation of stem cell renewal and hematopoiesis. Not surprisingly, mutations in the Notch gene have been linked to a number of types of malignancies. To better define the function of Notch in both normal and neoplastic hematopoiesis, a tetracycline-inducible system regulating expression of a ligand-independent, constitutively active form of Notch1 was introduced into murine E14Tg2a embryonic stem cells. During coculture, OP9 stromal cells induce the embryonic stem cells to differentiate first to hemangioblasts and subsequently to hematopoietic stem cells. Our studies indicate that activation of Notch signaling in flk + hemangioblasts dramatically reduces their survival and proliferative capacity and lowers the levels of hematopoietic stem cell markers CD34 and c-Kit and the myeloid marker CD11b. Global gene expression profiling of day 8 hematopoietic progenitors in the absence and presence of activated Notch yield candidate genes required for normal hematopoietic differentiation, as well as putative downstream targets of oncogenic forms of Notch including the noncanonical Wnts Wnt4 and 5A.
RE.CNT 76 THERE ARE 76 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 15 OF 58 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN DUPLICATE 4
AN 2008:4951 BIOSIS
DN PREV200800005155
TI mNotch1 signaling and erythropoietin cooperate in erythroid differentiation of multipotent progenitor cells and upregulate beta-globin.
AU Henning, Konstanze; Schroeder, Timm; Schwanbeck, Ralf; Rieber, Nikolaus; Bresnick, Emery H.; Just, Ursula [Reprint Author]
CS Univ Kiel, Dept Biochem, Olshaussenstr 40, D-24098 Kiel, Germany ujust@biochem.uni-kiel.de
SO Experimental Hematology (New York), (SEP 2007) Vol. 35, No. 9, pp. 1321-1332.

CODEN: EXHMA6. ISSN: 0301-472X.
DT Article
LA English
ED Entered STN: 12 Dec 2007
Last Updated on STN: 12 Dec 2007
AB Objective. In many developing tissues, signaling mediated by activation of the transmembrane receptor Notch influences cell-fate decisions, differentiation, proliferation, and cell survival. Notch receptors are expressed on hematopoietic cells and cognate ligands on bone marrow stromal cells. Here, we investigate the role of mNotch1 signaling in the control of erythroid differentiation of multipotent progenitor cells.Materials and Methods. Multipotent FDCP-mix cell lines engineered to permit the conditional induction of the constitutively active intracellular domain of mNotch1 (mNl1(IC)) by the 4-hydroxytamoxifen (OHT)-inducible system were used to analyze the effects of activated mNotch1 on erythroid differentiation and on expression of Gata1, Fog1, Eklf, NF-E2, and beta-globin. Expression was analyzed by Northern blotting and real-time polymerase chain reaction. Enhancer activity of reporter constructs was determined with the dual luciferase system in transient transfection assays.Results. Induction of mN1(IC) by OHT resulted in increased and accelerated differentiation of FDCP-mix cells along the erythroid lineage. Erythroid maturation was induced by activated Notch1 also under conditions that normally promote self-renewal, but required the presence of erythropoietin for differentiation to proceed. While induction of Notch signaling rapidly upregulated Hes1 and Hey1 expression, the expression of Gata1, Fog1, Eklf, and NF-E2 remained unchanged. Concomitantly with erythroid differentiation, activated mNotch1 upregulated beta-globin RNA. Notch signaling transactivated a reporter construct harboring a conserved RBP-J (CBF1) binding site in the hypersensitive site 2 (HS2) of human beta-globin. Transactivation by activated Notch was completely abolished when this

RBP-J site was mutated to prevent RBP-J binding.Conclusions. Our results
show that activation of mNotch1 induces erythroid differentiation in
cooperation with erythropoietin and upregulates,beta-globin expression.
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Elsevier Inc.

L3 ANSWER 16 OF 58 EMBASE COPYRIGHT (c) 2008 Elsevier B.V. All rights
reserved on STN
AN 2007415203 EMBASE
TI mNotch1 signaling and erythropoietin cooperate in erythroid
differentiation of multipotent progenitor cells and upregulate
β-globin.
AU Henning, Konstanze; Schwanbeck, Ralf; Just, Ursula (correspondence)
CS Department of Biochemistry, Christian-Albrechts University Kiel, Kiel,
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AU Schroeder, Timm; Rieber, Nikolaus; Just, Ursula (correspondence)
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AU Schroeder, Timm
CS Institute of Stem Cell Research, GSF-National Research Centre for
Environment and Health, Munich, Germany.
AU Bresnick, Emery H.
CS Department of Pharmacology, University of Wisconsin Medical School,
Madison, WI, United States.
SO Experimental Hematology, (Sep 2007) Vol. 35, No. 10, pp. 1321-1332.
Refs: 60
ISSN: 0301-472X CODEN: EXHEBH
PUI S 0301-472X(07)00325-6
CY United States
DT Journal; Article
FS 025 Hematology
029 Clinical and Experimental Biochemistry
LA English
SL English
ED Entered STN: 22 Apr 2008
Last Updated on STN: 22 Apr 2008
AB Objective: In many developing tissues, signaling mediated by activation of
the transmembrane receptor Notch influences cell-fate decisions,
differentiation, proliferation, and cell survival. Notch receptors are

expressed on hematopoietic cells and cognate ligands on bone marrow stromal cells. Here, we investigate the role of mNotch1 signaling in the control of erythroid differentiation of multipotent progenitor cells. Materials and Methods: Multipotent FDCP-mix cell lines engineered to permit the conditional induction of the constitutively active intracellular domain of mNotch1 (mN1(IC)) by the 4-hydroxytamoxifen (OHT)-inducible system were used to analyze the effects of activated mNotch1 on erythroid differentiation and on expression of Gata1, Fog1, Eklf, NF-E2, and β-globin. Expression was analyzed by Northern blotting and real-time polymerase chain reaction. Enhancer activity of reporter constructs was determined with the dual luciferase system in transient transfection assays. Results: Induction of mN1(IC) by OHT resulted in increased and accelerated differentiation of FDCP-mix cells along the erythroid lineage. Erythroid maturation was induced by activated Notch1 also under conditions that normally promote self-renewal, but required the presence of erythropoietin for differentiation to proceed. While induction of Notch signaling rapidly upregulated Hes1 and Hey1 expression, the expression of Gata1, Fog1, Eklf, and NF-E2 remained unchanged. Concomitantly with erythroid differentiation, activated mNotch1 upregulated β-globin RNA. Notch signaling transactivated a reporter construct harboring a conserved RBP-J (CBF1) binding site in the hypersensitive site 2 (HS2) of human β-globin. Transactivation by activated Notch was completely abolished when this RBP-J site was mutated to prevent RBP-J binding. Conclusions: Our results show that activation of mNotch1 induces erythroid differentiation in cooperation with erythropoietin and upregulates β-globin expression.

L3 ANSWER 17 OF 58 BIOSIS

AN 2008:218947 BIOSIS

DN PREV200800218989
TI Inhibition of the notch-delta pathway at early steps of endothelial progenitor differentiation impairs adhesion and spreading to the ECM via integrin modulation.
AU Caiado, Francisco [Reprint Author]; Real, Carla; Dias, Sergio
CS Ctr Invest Patol Mol, Inst Portugues Oncol Francisco Gentil, Angiogenesis Lab, Lisbon, Portugal
SO Blood, (NOV 16 2007) Vol. 110, No. 11, Part 1, pp. 1085A.
Meeting Info.: 49th Annual Meeting of the American-Society-of-Hematology.
Atlanta, GA, USA. December 08 -11, 2007. Amer Soc Hematol.
CODEN: BLOOAW. ISSN: 0006-4971.
DT Conference; (Meeting)
Conference; (Meeting Poster)
LA English
ED Entered STN: 26 Mar 2008
Last Updated on STN: 26 Mar 2008
AB Endothelial progenitor cells (EPC) have been proven essential in models of neoangiogenesis, where it was shown they differentiate at the angiogenesis site and incorporate the neo-vasculature. However, the mechanisms that mediate this differentiation process are not fully understood. Since members of the Notch-Delta (N-D) pathway are present on EPC (specifically N1, J1,J2 and D114), in this study, we exploited the possibility that N-D signaling might be involved in the early stages of EPC (bone marrow or humbilical chord blood derived) differentiation. First, using an optimized in vitro endothelial differentiation assay, the involvement of the N-D pathway in this process was evidenced by the increased expression of the downstream targets Hes1, Hey1 and Hey2 during EPC (Lin-, Sea-1+, Flk-1+/KDR+, CD133+ depending on the source) differentiation. We show that marine BM derived EPCs show a severe extracellular matrix (ECM) adhesion defect and a consequent impaired endothelial differentiation when exposed to Notch-Delta (N-D) pathway inhibitor (gamma-secretase inhibitor) during the first 6 days of endothelial differentiation. Early inhibition of the N-D pathway had no effect on BM derived EPC cells survival (apoptosis) or proliferation, although it reduced the number of adherent cells and inhibited their

differentiation into mature endothelial cells, as determined by the reduced number of LDL, vWE PE-CAM and Flk-1 positive cells. Similar results, evidencing a defect in EPC adhesion, were obtained from culturing BM derived EPC from D114(+/-) (heterozygous) mice. Transfection of BM derived EPC with a constitutively active form of Notch4 receptor promote their adhesion to the ECM and consequently increased the number of mature endothelial cells obtained at the end of the differentiation assay. These adhesion and spreading defects suggest an interplay between N-D pathway and integrin related pathways. Indeed, using human umbilical cord blood derived EPC, we show that early inhibition of N-D pathway leads to a decrease in a3 integrin surface expression, which strongly suggest a link with the EPC adhesion defect observed. In order to exploit the functional implications of this defect we sought to investigate whether N-D inhibition on BM-derived EpCs interfered with their ability to contribute towards endothelial recovery following wounding. Using a well established in vitro endothelial monolayer wounding assay, we observed that untreated EPCs adhere preferentially at the wounding site and to the endothelial cells at the wound leading edge, while EPCs treated with an N-D pathway inhibitor show a reduced ability to adhere at the wounding site, thus interfering with wound closure. Altogether these data suggest that N-D pathway is necessary for EPC eadothelial differentiation and that its inhibition interferes with their ability to adhere/spread to the ECM, possibly via integrin a3 activation and cytoskeletal modulation, and consequently to differentiate into mature endothelial cells interfering with the reendothelization process on wounded endothelium.

L3 ANSWER 18 OF 58 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN

AN 2008:218743 BIOSIS
DN PREV200800218785
TI Gene expression profiling of isolated mesenchymal and osteoblastic
cells exhibits a different pattern of expression in multiple myeloma
patients as compared to healthy subjects: Potential relationship with the
presence of bone lesions.
AU Giuliani, Nicola [Reprint Author]; Todoerti, Katia; Lisignoli, Gina;
Tagliaferri, Sara; Agnelli, Luca; Morandi, Francesca; Colla, Simona;
Crugnola, Monica; Magnani, Marina; Caramatti, Cecilia; Mangoni,
Marcellina; Deliliers, Giorgio Lambertenghi; Rizzoli, Vittorio; Neri,
Antonino
CS Univ Parma, I-43100 Parma, Italy
SO Blood, (NOV 16 2007) Vol. 110, No. 11, Part 1, pp. 1029A.
Meeting Info.: 49th Annual Meeting of the American-Society-of-Hematology.
Atlanta, GA, USA. December 08 -11, 2007. Amer Soc Hematol.
CODEN: BLOOAW. ISSN: 0006-4971.
DT Conference; (Meeting)
Conference; (Meeting Poster)
LA English
ED Entered STN: 26 Mar 2008
Last Updated on STN: 26 Mar 2008
AB Gene expression alterations occurring in the bone microenvironment cells and their potential relationships with the occurrence of bone lesions in multiple myeloma (MM) patients have never been investigated. In this study, we have isolated both mesenchymal (MSC) and osteoblastic (OB) cells, without in vitro differentiation, from bone biopsies obtained by iliac crest of 24 MM patients, 7 MGUS subjects and 8 healthy donors (N) who underwent orthopedics surgery. Bone status was evaluated in all MM patients by total X rays scan and MRI for the spine. Firstly, we evaluated cell proliferation in relationship with growth substrate (bone and glass) and cell phenotype by flow cytometry and immunohistochemistry. We found that both MSC and OB cells have higher cell doubling rate in MM patients as compared to N. Higher expression of alkaline phosphatase and Runx2 was observed in OB as compared to MSC cells in both N and MM patients without osteolytic lesions, but not in osteolytic ones. We performed a gene expression profiling analysis of isolated MSC and OB cells using GeneChip(R) Affymetrix

HG-U133A oligonucleotide arrays. An unsupervised analysis of the most variable genes across the dataset generated a hierarchical clustering with the two major branches containing respectively MSC and OB samples. A multiclass analysis of N, MGUS and MM patients identified 33 differentially expressed probe-set (specific for 27 genes) in MSC cells, and 19 differentially expressed probe-set (13 genes) in OB, and the identified transcripts mainly characterized N versus MM and MGUS samples. A supervised analysis between N and MM samples identified 65 probes (56 genes: 17 up-regulated and 39 down-regulated) differentially expressed in MSC and 35 probes (29 genes, 12 up-regulated and 17 down-regulated) in OB. Notably, genes encoding the Homeobox class proteins, such as HOXB2-6-7, were up-regulated in both MSC and OB of MM patients as compared to N. As regards the bone status, a total of 60 probe-sets (3 up-regulated and 57 down-regulated genes) were found differentially expressed in MSC from osteolytic, vs. non-osteolytic MM patients, whereas MGUS-MSC exhibited an intermediate transcriptional profile between osteolytic and non-osteolytic MM patients. A distinct:pattern of gene expression profiling was also observed in MSC versus OB when osteolytic and non-osteolytic MM patients were compared (26 vs. 94 differentially expressed probe-sets, respectively), including transcription factors related to MSC osteogenic differentiation belonging to Runx2 pathway (HEY1) or Writ and BMP signaling On the other hand. few genes were found differentially expressed in OB cells in relationship with the presence of bone lesions. In conclusion, we identified a distinctive transcriptional fingerprint in isolated MSC and OB cells of MM patients as compared to N subjects, which mainly correlated with cell proliferation. Moreover, a different gene expression profile was observed in MSC cells of MM patients according to the presence/absence of bone. lesions, highlighting the critical role of the block of the osteogenic differentiation.

L3 ANSWER 19 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN

AN 2007:627929 CAPLUS
DN 147:65048
TI BMP4 promotes formation of primitive vascular networks in human embryonic
stem cell-derived embryoid bodies
AU Boyd, N. L.; Dhara, S. K.; Rekaya, R.; Godbey, E. A.; Hasneen, K.; Rao, R.
R.; West, F. D., III; Gerwe, B. A.; Stice, S. L.
CS Regenerative Bioscience Center, University of Georgia, Athens, GA, 30602,
USA
SO Experimental Biology and Medicine (Maywood, NJ, United States) (2007),
232(6), 833-843
CODEN: EBMMBE; ISSN: 1535-3702
PB Society for Experimental Biology and Medicine
DT Journal
LA English
AB The vasculature develops primarily through two processes, vasculogenesis
and angiogenesis. Although much work has been published on angiogenesis,
less is known of the mechanisms regulating the de novo formation of the
vasculature commonly called vasculogenesis. Human embryonic stem cells
(hESC) have the capability to produce all of the cells of the body and
have been used as in vitro models to study the mol. signals controlling
differentiation and vessel assembly. One such regulatory mol. is
bone morphogenetic protein-4 (BMP4), which is required for
mesoderm formation and vascular/hematopoietic specification in several
species. However, hESC grown in feeder-free conditions and treated with
BMP4 differentiate into a cellular phenotype highly expressing a
trophoblast gene profile. Therefore, it is unclear what role, if any,
BMP4 plays in regulating vascular development in hESC. Here the authors
show in two National Institutes of Health-registered hESC lines (BG02 and
WA09) cultured on a 3D substrate of Matrigel in endothelial cell growth
medium-2 that the addition of BMP4 (100 ng/mL) for 3 days significantly
increases the formation and outgrowth of a network of cells reminiscent of
capillary-like structures formed by mature endothelial cells. Anal. of
the expression of 45 genes by quant. real time-polymerase chain reaction

on a low-d. array of the entire culture indicates a rapid and significant downregulation of pluripotent and most ectodermal markers with a general upregulation of endoderm, mesoderm, and endothelial markers. Of the genes assayed, BMPR2 and RUNX1 were differentially affected by exposure to BMP4 in both cell lines. Immunocytochem. indicates the morphol. structures formed were neg. for the mature endothelial markers CD31 and CD146 as well as the neural marker SOX2, yet pos. for the early vascular markers of endothelium (KDR, NESTIN) and smooth muscle cells (α-smooth muscle actin [αSMA]). Together, these data suggest BMP4 can enhance the formation and outgrowth of an immature vascular system.

RE.CNT 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 20 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN DUPLICATE 5
AN 2007:348876 CAPLUS
DN 147:49074
TI Hesr1 and Hesr2 regulate atrioventricular boundary formation in the developing heart through the repression of Tbx2
AU Kokubo, Hiroki; Tomita-Miyagawa, Sachiko; Hamada, Yoshio; Saga, Yumiko
CS Division of Mammalian Development, National Institute of Genetics, 1111 Yata, Mishima Shizuoka, 411-8540, Japan
SO Development (Cambridge, United Kingdom) (2007), 134(4), 747-755
CODEN: DEVPED; ISSN: 0950-1991
PB Company of Biologists Ltd.
DT Journal
LA English
AB The establishment of chamber specificity is an essential requirement for cardiac morphogenesis and function. Hesr1 (Hey1) and Hesr2 (Hey2) are specifically expressed in the atrium and ventricle, resp., implicating these genes in chamber specification. In our current study, we show that the forced expression of Hesr1 or Hesr2 in the entire cardiac lineage of the mouse results in the reduction or loss of the atrioventricular (AV) canal. In the Hesr1-misexpressing heart, the boundaries of the AV canal are poorly defined, and the expression levels of specific markers of

the AV myocardium, Bmp2 and Tbx2, are either very weak or undetectable.
More potent effects were observed in Hesr2-misexpressing embryos, in which
the AV canal appears to be absent entirely. These data suggest that Hesr1
and Hesr2 may prevent cells from expressing the AV canal-specific genes
that lead to the precise formation of the AV boundary. Our findings
suggest that Tbx2 expression might be directly suppressed by Hesr1 and
Hesr2. Furthermore, we find that the expression of Hesr1 and Hesr2 is
independent of Notch2 signaling. Taken together, our data demonstrate
that Hesr1 and Hesr2 play crucial roles in AV boundary formation through
the suppression of Tbx2.
RE.CNT 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 21 OF 58 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on
STN DUPLICATE 6
AN 2007:373380 BIOSIS
DN PREV200700370941
TI BMP-2 promotes differentiation of osteoblasts and chondroblasts
in Runx2-deficient cell lines.
AU Liu, Tingjiao; Gao, Yuhao; Sakamoto, Kei; Minamizato, Tokutaro; Furukawa,
Keizo; Tsukazaki, Tomoo; Shibata, Yasuaki; Bessho, Kazuhisa; Komori,
Toshihisa; Yamaguchi, Akira [Reprint Author]
CS Tokyo Med and Dent Univ, Grad Sch, Dept Oral Restitut, Sect Oral
Pathol,Bunkyo Ku, 1-5-45 Yushima, Tokyo 1138549, Japan
akira.mpa@tmd.ac.jp
SO Journal of Cellular Physiology, (JUN 2007) Vol. 211, No. 3, pp. 728-735.
CODEN: JCLLAX. ISSN: 0021-9541.
DT Article
LA English
ED Entered STN: 27 Jun 2007
Last Updated on STN: 27 Jun 2007
AB To investigate the molecular mechanism underlying the differentiation of
osteoblasts and chondroblasts, we established a clonal cell lines,
RD-C6, from Runx2-deficient mouse embryos. RD-C6 cells expressed almost
undetectable levels of phenotypes related to osteoblast and
chondroblast differentiation at basal culture condition, whereas treatment

with recombinant human bone morphogenetic protein-2 (rhBMP-2) or transduction of BMP-2 by adenovirus effectively induced this cell line to express mRNA related to the differentiation of osteoblasts and chondroblasts including alkaline phosphatase, osteocalcin, and osterix. Transduction of Runx2 also induced the expression of these mRNA in RD-C6 cells. BMP-2 transduction increased expression levels of mRNA for Msx2 and Dlx5, but Runx2 transduction induced no significant increases in expression levels of these mRNA. Microarray analysis using RD-C6 cells with or without rhBMP-2 treatment demonstrated that BMP-2 upregulated 66 genes including 13 transcription-related molecules such as Id1, Id2, Id4, Hey1 Smad6, Smad7, and Msx2. To confirm bone and cartilage formation ability of RD-C6 cells, we transplanted RD-C6 cells into the peritoneal cavity of athymic mice using diffusion chambers with rhBMP-2. RD-C6 cells generated unmineralized cartilage but not bone. These results indicate that BMP-2 induces Runx2-deficient cells to express markers related to osteoblast and chondroblast differentiation using a Runx2-independent pathway, but it failed to induce these cells to differentiate into bone-forming osteoblasts and mature chondrocytes.

L3 ANSWER 22 OF 58 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN DUPLICATE 7

AN 2007:203797 BIOSIS

DN PREV200700196794

TI CCN3/NOV inhibits BMP-2-induced osteoblast differentiation by interacting with BMP and Notch signaling pathways.

AU Minamizato, Tokutaro; Sakamoto, Kei; Liu, Tingjiao; Kokubo, Hiroki; Katsube, Ken-ichi; Perbal, Bernard; Nakamura, Seiji; Yamaguchi, Akira [Reprint Author]

CS Tokyo Med and Dent Univ, Grad Sch, Sect Oral Pathol, Bunkyo Ku, 1-5-45 Yushima, Tokyo 1138549, Japan akira.mpa@tmd.ac.jp

SO Biochemical and Biophysical Research Communications, (MAR 9 2007) Vol. 354, No. 2, pp. 567-573. CODEN: BBRCA9. ISSN: 0006-291X.

DT Article

LA English

ED Entered STN: 21 Mar 2007
Last Updated on STN: 21 Mar 2007
AB We elucidate the role of CCN3/NOV, a member of the CCN family proteins, in
osteoblast differentiation using MC3T3-E1 osteoblastic
cells. Transduction with CCN3 adenovirus (AdCCN3) alone induced no
apparent changes in the expression of osteoblast-related
markers, whereas cotransduction with BMP-2 adenovirus (AdBMP-2) and AdCCN3
significantly inhibited the AdBMP-2-induced mRNA expression of Runx2,
osterix, ALP, and osteocalcin. Immunoprecipitation-western
analysis revealed that CCN3 associated with BMP-2. Compared to
transduction with AdBMP-2 alone, cotransduction with AdBMP-2 and AdCCN3
attenuated the expression of phosphorylated Smad1/5/8 and the mRNA for
Id1, M2, and M3. Transduction with AdCCN3 stimulated the expression of
cleaved Notch1, the mRNA expression of Hes1 and Hey1/Hesr1, and
the promoter activities of Hes1 and Hey1. The inhibitory
effects of CCN3 on the expression of BMP-2-induced osteoblast
-related markers were nullified in Hey1-deficient
osteoblastic cells. These results indicate that CCN3 exerts
inhibitory effects on BMP-2-induced osteoblast differentiation
by its involvement of the BMP and Notch signaling pathways. (c) 2007
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L3 ANSWER 23 OF 58 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on
STN
AN 2007:299730 BIOSIS
DN PREV200700304858
TI EWS-FLI1 interferes with p53-dependent growth control in Ewing's sarcoma
by suppressing autostimulation of the NOTCH pathway.
AU Ban, Jozef [Reprint Author]; Schaefer, Karl-Ludwig; Kreppel, Michael;
Bachmaier, Radostina; Kovar, Heinrich
CS Childrens Canc Res Inst, Vienna, Austria
SO Proceedings of the American Association for Cancer Research Annual
Meeting, (APR 2007) Vol. 48, pp. 501.
Meeting Info.: 98th Annual Meeting of the American-Association-for-Cancer-
Research. Los Angeles, CA, USA. April 14 -18, 2007. Amer Assoc Canc Res.
ISSN: 0197-016X.
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)

LA English
ED Entered STN: 9 May 2007
Last Updated on STN: 9 May 2007

L3 ANSWER 24 OF 58 EMBASE COPYRIGHT (c) 2008 Elsevier B.V. All rights
reserved on STN
AN 2007309673 EMBASE
TI Notch signaling in development and cancer.
AU Bolos, Victoria; Grego-Bessa, Joaquin; De La Pompa, Jose Luis (correspondence)
CS Departmento de Inmunologia Y Oncologia, Centro Nacional de Biotecnologia/Consejo Superior de Investigaciones Cientificas, E-28049
Madrid, Spain. jlpompa@cnb.uam.es
AU De La Pompa, Jose Luis (correspondence)
CS Departmento de Inmunologia Y Oncologia, Centro Nacional de Biotecnologia/Consejo Superior de Investigaciones Cientificas, Campus de
Cantoblanco, Darwin 3, E-28049 Madrid, Spain. jlpompa@cnb.uam.es
SO Endocrine Reviews, (May 2007) Vol. 28, No. 3, pp. 339-363.
Refs: 296
ISSN: 0163-769X E-ISSN: 0163-769X CODEN: ERVIDP
CY United States
DT Journal; General Review; (Review)
FS 016 Cancer
021 Developmental Biology and Teratology
029 Clinical and Experimental Biochemistry
003 Endocrinology
005 General Pathology and Pathological Anatomy
LA English
SL English
ED Entered STN: 17 Jul 2007
Last Updated on STN: 17 Jul 2007
AB Notch is an evolutionarily conserved local cell signaling mechanism that
participates in a variety of cellular processes: cell fate specification,
differentiation, proliferation, apoptosis, adhesion, epithelial-
mesenchymal transition, migration, and angiogenesis. These processes can
be subverted in Notch-mediated pathological situations. In the first part
of this review, we will discuss the role of Notch in vertebrate central
nervous system development, somitogenesis, cardiovascular and endocrine
development, with attention to the mechanisms by which Notch regulates
cell fate specification and patterning in these tissues. In the second
part, we will review the molecular aspects of Notch-mediated neoplasias,

where Notch can act as an oncogene or as a tumor suppressor. From all these studies, it becomes evident that the outcome of Notch signaling is strictly context-dependent and differences in the strength, timing, cell type, and context of the signal may affect the final outcome. It is essential to understand how Notch integrates inputs from other signaling pathways and how specificity is achieved, because this knowledge may be relevant for future therapeutic applications.

L3 ANSWER 25 OF 58 CAPLUS
AN 2007:908664 CAPLUS
DN 148:24664
TI Regulation of the expression of FGF receptors and extracellular matrix associated genes in ATDC5 chondroprogenitor cells
AU Lee, Sung-Jin; Kim, Jong-Pyl; Kim, Yong-Min; Park, Kyung-Jin; Kim, Hye-Ryun; Kim, Seung-Ryul; Lee, Hak-Kyo; Choi, Joong-Kook
CS Gyeonggi Regional Research Center, Hankyong National University, Gyeonggi, 456-749, S. Korea
SO Korean Journal of Genetics (2007), 29(2), 263-274
CODEN: KJGEDG; ISSN: 0254-5934
PB Genetics Society of Korea
DT Journal
LA English
AB Ordered processes of proliferation, differentiation and maturation of mesenchymal stem cells are required for chondrogenesis and the development of long bones. In vertebrate, Hedgehog (Hh) proteins are known to be involved in many key developmental processes such as chondrogenesis and bone development. However, mol. mechanism governing these processes, especially at the early stage, remains poorly characterized. We employed a mouse Illumina chip array to examine temporal expression patterns of cellular genes that are critically regulated by SHH in mouse chondroprogenitor cell line- ATDC5. The data from the DNA chip assay and RT-PCR anal. suggests that SHH controls the expression of a set of genes

involved in FGF signaling and remodeling of extracellular matrix.
RE.CNT 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 26 OF 58 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on
STN
AN 2008:214147 BIOSIS
DN PREV200800225906
TI CCN3/NOV inhibits BMP-2-induced osteoblast differentiation by interacting with BMP and notch signaling pathways.
AU Minamizato, T. [Reprint Author]; Sakamoto, K.; Nakamura, S.; Yamaguchi, A.
CS Tokyo Med and Dent Univ, Grad Sch, Sect Oral Pathol, Tokyo, Japan
SO Journal of Bone and Mineral Research, (SEP 2007) Vol. 22, No. Suppl. 1,
pp. S249.
Meeting Info.: 29th Annual Meeting of the American-Society-for-Bone-and-
Mineral-Research. Honolulu, HI, USA. September 16 -19, 2007. Amer Soc Bone
& Mineral Res.
CODEN: JBMREJ. ISSN: 0884-0431.
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LA English
ED Entered STN: 26 Mar 2008
Last Updated on STN: 26 Mar 2008

L3 ANSWER 27 OF 58 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on
STN DUPLICATE 8
AN 2007:249216 BIOSIS
DN PREV200700247032
TI Inhibition of gamma-secretases alters both proliferation and differentiation of mesenchymal stem cells.
AU Vujovic, S.; Henderson, S. R.; Flanagan, A. M.; Clements, M. O. [Reprint
Author]
CS Univ Westminster, Sch Biosci, 115 New Cavendish St, London W1W 6UW, UK
clemenm@wmin.ac.uk
SO Cell Proliferation, (APR 2007) Vol. 40, No. 2, pp. 185-195.
ISSN: 0960-7722.
DT Article
LA English
ED Entered STN: 18 Apr 2007
Last Updated on STN: 18 Apr 2007
AB Introduction: Human mesenchymal stem cell (hMSC) proliferation and
development is regulated by many signalling pathways. gamma-Secretases

play an important role in Notch signalling as well as other processes that are involved in developmental decisions, but their role in hMSC proliferation and cell fate decisions has not been explored. Objective: To investigate the role of gamma-secretases in hMSC proliferation and differentiation. Materials and methods: Using the gamma-secretase inhibitor N-[N-(3,5-Difluorophenacetyl-L-alanyl]-S-phenylglycine t-butyl ester (DAPT), we investigated their role in hMSC growth and differentiation to chondrogenic, osteogenic and adipogenic fates. Results: We found that inhibiting gamma-secretases reduced the rate of hMSC proliferation, and altered hMSC differentiation in vitro. Addition of DAPT had an inhibitory effect on chondrogenesis resulting in impaired cartilage matrix production and altered chondrocyte morphology. DAPT treated chrodrocytic pellets had reduced levels of Hes1 and Hey1 suggesting that these effects are mediated via Notch signalling. Addition of the DAPT inhibitor to osteogenic cultures did not alter the appearance of bone markers, however, adipogenesis occurred in these cultures in a DAPT concentration-dependent manner. DAPT did not enhance adipogenesis in the presence of a potent adipogenic cocktail, but had an adipogenic effect when combined with dexamethasone only. Conclusion: We conclude that gamma-secretases play an important role in both hMSC proliferation and differentiation.

L3 ANSWER 28 OF 58 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN

AN 2008:254033 BIOSIS

DN PREV200800257452

TI EWS-FLI1 controls cell cycle and death by suppressing distinct signalling pathways converging on p53.

AU Ban, J. [Reprint Author]; Aryee, D. N. T.; Bennani, I.; Kovar, H.

CS St Anna Childrens Hosp, Childrens Canc Res Inst, A-1090 Vienna, Austria

SO FEBS Journal, (JUL 2007) Vol. 274, No. Suppl. 1, pp. 155. Meeting Info.: 32nd Congress of the Federation-of-European-Biochemical-Societies (FEBS). Vienna, AUSTRIA. July 07 -12, 2007. Federat European Biochem Soc.

ISSN: 1742-464X. E-ISSN: 1742-4658.
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LA English
ED Entered STN: 9 Apr 2008
Last Updated on STN: 9 Apr 2008

L3 ANSWER 29 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2006:1225943 CAPLUS
DN 146:5717
TI Gene expression signatures associated with oncogenic pathway deregulation
and their use in the selection of antitumor therapy
IN Nevins, Joseph R.; Bild, Andrea H.; Yao, Guang; Chang, Jeffrey T.; Wang,
Quanli; Potti, Anil; Harpole, David; Lancaster, Johnathan M.; Berchuck,
Andrew; Olson, John A., Jr.; Marks, Jeffrey R.; West, Mike; Dressman,
Holly
PA Duke University, USA
SO PCT Int. Appl., 109pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2006124836	A1	20061123	WO 2006-US18827	20060515
WO 2006124836	A9	20080228		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR,
KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX,
MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE,
SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC,
VN, YU, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ,
CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH,

GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA
CA 2608359 A1 20061123 CA 2006-2608359 20060515
EP 1910564 A1 20080416 EP 2006-759888 20060515
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR
PRAI US 2005-680490P P 20050513
WO 2006-US18827 W 20060515
AB The disclosure relates to identifying deregulated signal transduction pathways and their use in the diagnosis of cancer. In certain embodiments, the methods of the disclosure can be used to evaluate therapeutic agents for the treatment of cancer. Candidate genes were identified in human primary mammary epithelial cells by transforming them with a series of oncogenic adenovirus and observing changes in gene expression profiles. These were then validated in mouse models.
RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 30 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2006:437488 CAPLUS
DN 144:466043
TI Gene expression profiling in the diagnosis, prognosis, and classification of acute myeloid leukemia and selection of therapies
IN Haferlach, Torsten; Dugas, Martin; Kern, Wolfgang; Kohlmann, Alexander; Schnittger, Susanne; Schoch, Claudia
PA Roche Diagnostics G.m.b.H., Germany; F. Hoffmann-La Roche A.-G.; Ludwig-Maximilians- Universitaet
SO PCT Int. Appl., 455 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006048262	A2	20060511	WO 2005-EP11728	20051103
WO 2006048262	A3	20060824		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,

CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR,
KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX,
MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE,
SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC,
VN, YU, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ,
CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH,
GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
KG, KZ, MD, RU, TJ, TM
EP 1809765 A2 20070725 EP 2005-802544 20051103
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR
PRAI US 2004-625238P P 20041104
US 2004-625244P P 20041104
US 2004-625266P P 20041104
US 2004-625314P P 20041104
US 2004-625623P P 20041104
US 2004-625692P P 20041104
US 2004-625696P P 20041104
WO 2005-EP11728 W 20051103
AB A to rapid and reliable approaches to leukemia diagnosis and prognosis by
anal. of gene expression profiles is demonstrated. Changes in gene
expression that are correlated with different chromosomal translocations
associated with acute myeloid leukemia are identified. In addition to methods,
the invention also provides related kits and systems.

L3 ANSWER 31 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN DUPLICATE 9
AN 2006:1305553 CAPLUS
DN 146:59139
TI Developmental patterning of the cardiac atrioventricular canal by Notch
and Hairy-related transcription factors
AU Rutenberg, Joshua B.; Fischer, Andreas; Jia, Haibo; Gessler, Manfred;

Zhong, Tao P.; Mercola, Mark
CS Burnham Institute for Medical Research, La Jolla, CA, 92037, USA
SO Development (Cambridge, United Kingdom) (2006), 133(21), 4381-4390
CODEN: DEVPED; ISSN: 0950-1991
PB Company of Biologists Ltd.
DT Journal
LA English
AB Mutations in Notch2, Jagged1 or homologs of the Hairy-related transcriptional repressor Hey2 cause congenital malformations involving the non-chamber atrioventricular canal (AVC) and inner curvature (IC) regions of the heart, but the underlying mechanisms have not been investigated. By manipulating signaling directly within the developing chick heart, the authors demonstrated that Notch2, Hey1 and Hey2 initiate a signaling cascade that delimits the non-chamber AVC and IC regions. Specifically, misactivation of Notch2 signaling, or misexpression of either Hey1 or Hey2, repressed Bmp2. Because Jagged (also known as Serrate in non-mammalian species) ligands were found to be present in prospective chamber myocardium, these data support the model that Notch2 and Hey proteins cause the progressive restriction of Bmp2 expression to within the developing AVC and IC, where it is essential for differentiation. Misactivation or inhibition of Notch2 specifically induced or inhibited Hey1, resp., but these manipulations did not affect Hey2, implicating Hey1 as the direct mediator of Notch2. Bmp2 within the developing AVC and IC has been shown to induce Tbx2, and the authors found that Tbx2 misexpression inhibited the expression of both Hey1 and Hey2. Tbx2, therefore, is envisaged to constitute a feedback loop that sharpens the border with the developing AVC and IC by delimiting Hey gene expression to within prospective chamber regions. Anal. of the loss-of-function phenotype in mouse embryos homozygous for targeted disruption of Hey2 revealed an expanded AVC domain of Bmp2. Similarly, zebrafish gridlock (Hey2 homolog) mutant embryos showed ectopic expression of Bmp4, which normally marks AVC myocardium in this species. Thus, Hey pathway regulation of cardiac Bmp appears to be an evolutionarily conserved mechanism to delimit AVC and IC fate, and

provides a potential mechanistic explanation for cardiac malformations caused by mutations in Serrate/Jagged1 and Notch signaling components.
RE.CNT 82 THERE ARE 82 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 32 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2007:47473 CAPLUS
DN 147:116411
TI Bone marrow transplantation attenuates the myopathic phenotype of a muscular mouse model of spinal muscular atrophy
AU Salah-Mohellibi, Nouzha; Millet, Gaelle; Andre-Schmutz, Isabelle; Desforges, Benedicte; Olaso, Robert; Roblot, Natacha; Courageot, Sabrina; Bensimon, Gilbert; Cavazzana-Calvo, Marina; Melki, Judith
CS Molecular Neurogenetics Laboratory, Institut National de la Sante et de la Recherche Medicale, Inserm, U798, Evry, F-91057, Fr.
SO Stem Cells (Durham, NC, United States) (2006), 24(12), 2723-2732
CODEN: STCEEJ; ISSN: 1066-5099
PB AlphaMed Press
DT Journal
LA English
AB Bone marrow (BM) transplantation was performed on a muscular mouse model of spinal muscular atrophy that had been created by mutating the survival of motor neuron gene (Smn) in myofibers only. This model is characterized by a severe myopathy and progressive loss of muscle fibers leading to paralysis. Transplantation of wild-type BM cells following irradiation at a low dose (6 Gy) improved motor capacity (+85%). This correlated with a normalization of myofiber number associated with a higher number of regenerating myofibers (1.6-fold increase) and an activation of CD34 and Pax7 satellite cells. However, BM cells had a very limited capacity to replace or fuse to mutant myofibers (2%). These data suggest that BM transplantation was able to attenuate the myopathic phenotype through an improvement of skeletal muscle regeneration of recipient mutant mice, a process likely mediated by a biol. activity of BM-derived cells. This hypothesis was further supported by the capacity of muscle protein exts. from transplanted mutant mice to promote myoblast proliferation in vitro

(1.6-fold increase). In addition, a tremendous upregulation of hepatocyte growth factor (HGF), which activates quiescent satellite cells, was found in skeletal muscle of transplanted mutants compared with nontransplanted mutants. Eventually, thanks to the Cre-loxP system, we show that BM-derived muscle cells were strong candidates harboring this biol. activity. Taken together, our data suggest that a biol. activity is likely involved in muscle regeneration improvement mediated by BM transplantation. HGF may represent an attractive paracrine mechanism to support this activity.
RE.CNT 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 33 OF 58 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN DUPLICATE 10
AN 2006:236950 BIOSIS
DN PREV200600238930
TI Comparative genomics on HHIP family orthologs.
AU Katoh, Yuriko; Katoh, Masaru [Reprint Author]
CS Natl Canc Ctr, Res Inst, Genet and Cell Biol Sect, Chuo Ku, 5-1-1 Tsukiji, Tokyo 1040045, Japan
mkatoh@ncc.go.jp
SO International Journal of Molecular Medicine, (FEB 2006) Vol. 17, No. 2, pp. 391-395.
ISSN: 1107-3756.
DT Article
LA English
OS GenBank-NP071920.1; EMBL-NP071920.1; DDJB-NP071920.1; GenBank-NM032425.3; EMBL-NM032425.3; DDJB-NM032425.3; GenBank-NM024746.2; EMBL-NM024746.2; DDJB-NM024746.2; GenBank-NP079022.1; EMBL-NP079022.1; DDJB-NP079022.1; GenBank-NM020259.3; EMBL-NM020259.3; DDJB-NM020259.3; GenBank-NM030175.1; EMBL-NM030175.1; DDJB-NM030175.1; GenBank-AC107504.4; EMBL-AC107504.4; DDJB-AC107504.4; GenBank-AC094820.6; EMBL-AC094820.6; DDJB-AC094820.6; GenBank-AC134264.2; EMBL-AC134264.2; DDJB-AC134264.2
ED Entered STN: 19 Apr 2006
Last Updated on STN: 19 Apr 2006
AB Hedgehog, FGF, VEGF, and Notch signaling pathways network together for

vascular remodeling during embryogenesis and carcinogenesis. HHIP1 (HHIP)
is an endogenous antagonist for SHH, IHH, and DHH. Here, comparative
integromics analyses on HHIP family members were performed by using
bioinformatics and human intelligence. HHIP1, HHIP2 (HHIPL1 or KIAA1822)
and HHIP3 (HHIPL2 or KIAA1822L) constitute human HHIP gene family. Rat
Hhip1, Hhip2, and Hhip3 genes were identified within AC107504.4,
AC094820.6, and AC134264.2 genome sequences, respectively.
HHIP-homologous (HIPH) domain with conserved 18 Cys residues was
identified as the novel domain conserved among mammalian HHIP1, HHIP2, and
HHIP3 orthologs. HHIP1 mRNA was expressed in coronary artery endothelial
cells, prostate, and rhabdomyosarcoma. HHIP2 mRNA was expressed in
trabecular bone cells. HHIP3 mRNA was expressed in testis,
thyroid gland, osteoarthritic cartilarge, pancreatic cancer, and
lung cancer. Promoters of HHIP family genes were not well conserved
between human and rodents. Although GLI-, CSL-, and HES/HEY-binding sites
were not identified, eleven bHLH-binding sites were identified within
human HHIP1 promoter. Expression of HES/ HEY family members, including
HES1, HES2, HES3, HES4, HES5, HES6, HES7, HEY1, HEY2 and HEYL,
in coronary artery endothelial cells was not detected in silico.
Up-regulation of HHIP1 due to down-regulation of Notch-CSL-HES/HEY
signaling cascade repressing bHLH transcription factors results in
down-regulation of the Hedgehog-VEGF-Notch signaling cascade. On the
other hand, down-regulation of HHIP1 due to up-regulation of Notch
signaling in vascular endothelial cells during angiogenesis results in
up-regulation of the Hedgehog-VEGF-Notch signaling cascade. Because HHIP1
is the key molecule for vascular remodeling, HHIP1 is the pharmacogenomics
target in the fields of oncology and vascular medicine.

AN 2007:98064 BIOSIS
DN PREV200700103571

TI BMP-2 induces Hey1 and HES1 in osteoblastic cells via Notch-dependent and - Independent signaling pathways.
AU Vukcevic, M. [Reprint Author]; Zamurovic, N.; Luong-Nguyen, N.; Geffers, I.; Gossler, A.; Susa, M.
CS Novartis Inst BioMed Res, Basel, Switzerland
SO Journal of Bone and Mineral Research, (SEP 2006) Vol. 21, No. Suppl. 1, pp. S384.
Meeting Info.: 28th Annual Meeting of the American-Society-for-Bone-and-Mineral-Research. Philadelphia, PA, USA. September 15 -19, 2006. Amer Soc Bone & Mineral Res.
CODEN: JBMREJ. ISSN: 0884-0431.
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LA English
ED Entered STN: 7 Feb 2007
Last Updated on STN: 7 Feb 2007

L3 ANSWER 35 OF 58 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
AN 2007:98061 BIOSIS
DN PREV200700103568
TI Identification of a novel zinc finger protein that modulates Notch signaling.
AU Sakamoto, K. [Reprint Author]; Yamaguchi, A.
CS Tokyo Med and Dent Univ, Tokyo, Japan
SO Journal of Bone and Mineral Research, (SEP 2006) Vol. 21, No. Suppl. 1, pp. S383.
Meeting Info.: 28th Annual Meeting of the American-Society-for-Bone-and-Mineral-Research. Philadelphia, PA, USA. September 15 -19, 2006. Amer Soc Bone & Mineral Res.
CODEN: JBMREJ. ISSN: 0884-0431.
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LA English
ED Entered STN: 7 Feb 2007
Last Updated on STN: 7 Feb 2007

L3 ANSWER 36 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2006:158282 CAPLUS
DN 144:305696
TI Transcriptional profiling implicates TGFβ/BMP and Notch signaling pathways in ductular differentiation of fetal murine hepato-blasts

AU Ader, Tammy; Norel, Raquel; Levoci, Lauretta; Rogler, Leslie E.
CS Marion Bessin Liver Research Center, Department of Medicine, Albert
Einstein College of Medicine, Bronx, NY, 10461, USA
SO Mechanisms of Development (2006), 123(2), 177-194
CODEN: MEDVE6; ISSN: 0925-4773
PB Elsevier B.V.
DT Journal
LA English
AB Bile duct morphogenesis involves sequential induction of biliary specific
gene expression, bilayer generation, cell proliferation, remodeling and
apoptosis. WBC-3 cells are a model system to study differentiation of
hepatoblasts along the hepatocytic or bile ductular lineage in vitro and
in vivo. We used microarray to define mol. pathways during ductular
differentiation in response to Matrigel. The temporal pattern of
expression of marker genes induced was similar to that observed during bile
duct formation in vivo. Notch, HNF1β, Polycystic kidney disease 2,
Bicaudal C 1 and β-catenin were up regulated during the time course.
Functional clustering anal. revealed significant up regulation of clusters
of genes involved in extracellular matrix remodeling, ion transport,
vacuoles, lytic vacuoles, pro-apoptotic and anti-apoptotic genes,
transcription factors and neg. regulators of the cell proliferation, while
genes involved in the cell cycle were significantly down regulated. Notch
signaling pathway was activated by treatment with Matrigel. In addition,
TGFβ/BMP signaling pathway members including the type I TGFβ
receptor and Smads 3, 4 and 5 were significantly up regulated, as were
several TGFβ/BMP responsive genes including Hey 1
, a regulator of Notch pathway signaling. SMADS 3, 4 and 5 were present
in the nuclear fraction of HBC-3 cells during ductular differentiation in
vitro, but not during hepatocyte differentiation. SMAD 5 was
preferentially expressed in hepatoblasts undergoing bile duct
morphogenesis in the fetal liver, while the TGFβ/BMP signaling
antagonist chordin, was expressed throughout the liver suggesting a
mechanism by which TGFβ/BMP signaling is limited to hepatoblasts that

contact portal mesenchyme in vivo.
RE.CNT 57 THERE ARE 57 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 37 OF 58 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on
STN
AN 2007:107565 BIOSIS
DN PREV200700113008
TI Who are the players in the neighborhood: Signaling pathways in the
hematopoietic stem cell niche.
AU Paz, H. [Reprint Author]; Shafizadeh, H.; Lynch, M.; Ganapati, U.; Gasson,
J. C.
CS Univ Calif Los Angeles, Sch Med, Los Angeles, CA USA
SO Experimental Hematology (New York), (SEP 2006) Vol. 34, No. 9, Suppl. 1,
pp. 72.
Meeting Info.: 35th Annual Meeting of the International-Society-for-
Experimental-Hematology. Minneapolis, MN, USA. September 27 -30, 2006. Int
Soc Expert Hemat.
CODEN: EXHMA6. ISSN: 0301-472X.
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LA English
ED Entered STN: 14 Feb 2007
Last Updated on STN: 14 Feb 2007

L3 ANSWER 38 OF 58 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on
STN
AN 2007:96807 BIOSIS
DN PREV200700102314
TI Overexpression of Heyl, a notch target gene, leads to osteopenia in mice due to decreased osteoblast performance.
AU Susa, M. [Reprint Author]; Zamurovic, N.; Salie, R.; Rohner, D.; Evans,
G.; Vukcevic, M.; Mueller, M.; Kinzel, B.; Kneissel, M.
CS Novartis Inst BioMed Res, Basel, Switzerland
SO Journal of Bone and Mineral Research, (SEP 2006) Vol. 21, No. Suppl. 1,
pp. S57.
Meeting Info.: 28th Annual Meeting of the American-Society-for-Bone-and-
Mineral-Research. Philadelphia, PA, USA. September 15 -19, 2006. Amer Soc
Bone & Mineral Res.
CODEN: JBMREJ. ISSN: 0884-0431.
DT Conference; (Meeting)

Conference; Abstract; (Meeting Abstract)
LA English
ED Entered STN: 7 Feb 2007
Last Updated on STN: 7 Feb 2007

L3 ANSWER 39 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN DUPLICATE 11
AN 2005:713955 CAPLUS
DN 143:187909
TI Methods of using databases to create gene-expression microarrays, equine
and canine microarrays created thereby, and uses of the microarrays
IN Bertone, Alicia; Gu, Weisong
PA The Ohio State University, USA
SO PCT Int. Appl., 1475 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2005067649	A2	20050728	WO 2005-XA517	20050107
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
WO 2005067649	A2	20050728	WO 2005-US517	20050107
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,				

GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT,
RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML,
MR, NE, SN, TD, TG
PRAI US 2004-535111P P 20040108
WO 2005-US517 A 20050107
AB Methods of preparing biol. databases, and databases prepared according to those
methods. The methods can be performed entirely using computer resources,
relying solely on publicly available biol. sequence information, and can
be used to generate species-specific nucleic acid microarrays. The
approach involves two major steps: identification of the 3' coding domains
(CDSs) and 3' expressed sequence tags (ESTs) in public domain sequence
databases and subsequent annotation of the sequences. For the algorithm
using 20,022 equine sequences in GenBank (June, 2003), the 3' equine CDSs
are identified by selecting the full and partial CDSs that have a stop
codon at the 3' end. This approach ensures that sequences selected are
anchored to the 3' end; most contain the 3' untranslated region (UTR),
which is more species-specific, compared with the coding region. Use of
the UTR sequence in probe design is an asset for improvement of microarray
accuracy. An algorithm analyzes the partial equine CDSs and ESTs with
those in a human-mouse CDS database (a subset of the GenBank nonredundant
database) in order to provide annotation to the selected 3' equine
sequences. A total of 3099 equine 3' coding sequences and 3' ESTs are

selected for the equine-specific gene expression array, and 68,266 oligonucleotide probes designed according to Affymetrix's chip design guide. Microarray anal. identified genes expressed in equine synoviocytes in the absence and presence of lipopolysaccharide, as well as differentially expressed genes in developmental orthopedic disease (osteochondrosis desiccans and cervical vertebral malformation), equine osteoarthritis, equine protozoal myelitis, herpes virus-1 infection, potentially compromising stress, and laminitis in horses. Analogous methods are used to generate a canine-specific microarray to detect gene expression during osteoarthritis in dogs. [This abstract record is one of two records for this document necessitated by the large number of index entries required to fully index the document and publication system constraints.].

L3 ANSWER 40 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2005:902703 CAPLUS
DN 143:272498
TI Gene expression profiles in the diagnosis and treatment of Alzheimer's disease
IN Landfield, Philip W.; Porter, Nada M.; Chen, Kuey Chu; Geddes, James; Blalock, Eric
PA University of Kentucky Research Foundation, USA
SO PCT Int. Appl., 114 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005076939	A2	20050825	WO 2005-US3668	20050209
WO 2005076939	A3	20060706		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,

NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, SM
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT,
RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML,
MR, NE, SN, TD, TG
US 20070082350 A1 20070412 US 2006-501226 20060809
PRAI US 2004-542281P P 20040209
WO 2005-US3668 A 20050209
AB Genes showing altered patterns of expression in the brain that are associated with the neurol. changes found in Alzheimer's disease and that can be used in the early diagnosis of the disease, including the incipient form of the disease, are identified. The methods and kits of the invention utilize a set of genes and their encoded proteins that are shown to be correlated with incipient Alzheimer's disease.

L3 ANSWER 41 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2005:523621 CAPLUS
DN 143:54416
TI DNA microarray for identifying genes regulated by basal transcription factors and biomarkers for treating diseases through regulation of hepatocyte nuclear factors
IN Odom, Duncan T.; Young, Richard A.
PA Whitehead Institute for Biomedical Research, USA
SO PCT Int. Appl., 113 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005054461	A2	20050616	WO 2004-US39805	20041123
WO 2005054461	A3	20050909		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,

CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL, PL, PT, RO,
SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR,
NE, SN, TD, TG

US 20050239106	A1	20051027	US 2004-996240	20041123
GB 2422837	A	20060809	GB 2006-10482	20041123
DE 112004002318	T5	20070118	DE 2004-112004002318	20041123
JP 2007515954	T	20070621	JP 2006-541476	20041123
PRAI US 2003-525318P	P	20031126		
US 2004-542520P	P	20040206		
US 2004-544835P	P	20040213		
US 2004-547933P	P	20040226		
WO 2004-US39805	W	20041123		

AB The invention relates to transcriptional regulators and related methods thereof. Determining genes from a subset of genes that are regulated by a transcriptional regulator is achieved by (a) selectively isolating chromatin from a cell; (b) selectively isolating chromatin fragments which are bound by the transcriptional regulator; (3) amplifying both the bound chromatin fragments and isolated chromatin to generate amplified chromatin fragments and amplified control chromatin, resp.; (4) hybridizing the amplified control and the amplified fragments to a DNA microarray; and (5) determining and comparing a hybridization signal at each of the spots on the microarray between those generated by the amplified control chromatin and

the amplified chromatin fragments. The DNA microarray for determining promoter occupancy in a human cell, comprises (1) at least 10,000 experiment spots, each comprising a promoter region from a human gene; and (2) at least 100 control spots, each control spot comprising a non-promoter region. Applicants selected 15,000 cDNAs from the NCBI RefSeq database, mapped them to NCBI Build 22 of the human genome using BLAST, and amplified sequences from the genomic region -750 bp to +250 bp relative to the transcriptional start site. The invention also identifies genes regulated/occupied by the transcription factors HNF-1α, HNF-4α, and HNF-6 in human hepatocytes and pancreatic islets. Thus, the invention relates to the identification of genes regulated by transcriptional regulators, to the treatment of diseases associated with abnormal function of a transcriptional regulator, and to the modulation of gene expression, including genes expressed in hepatocytes or pancreatic cells, through the modulation of transcriptional regulator activity.

L3 ANSWER 42 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2005:1020555 CAPLUS
DN 143:320266
TI Genes with differential expression profile between human dental pulp stem cells and mesenchymal stem cells and use for regenerating tooth germ
IN Ueda, Minoru; Yamada, Yoichi
PA Hitachi Medical Corp., Japan
SO Jpn. Kokai Tokkyo Koho, 246 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2005253442	A	20050922	JP 2004-111582	20040309

PRAI JP 2004-111582 20040309
AB The present invention relates to a group of genes whose expression profile are different between human dental pulp stem cells and mesenchymal stem

cells, as well as a method for regenerating tooth germ using these genes.

According to the present invention, the gene expression profiles and cluster anal. between human dental pulp stem cells (hDPSCs) and mesenchymal stem cells (hMSCs) as representative populations of odontoprogenitor and osteoprogenitor cell were revealed, and a group of genes whose expression profile are different between human dental pulp stem cells and mesenchymal stem cells was identified. By utilizing the groups of the genes of the present invention together with the dental pulp stem cells and mesenchymal stem cells, hard tissue such as tooth germ, dental pulp, dentin or bone can be regenerated. The present inventors investigated the gene expression profiles and cluster anal. between human dental pulp stem cells (hDPSCs) and mesenchymal stem cells (hMSCs) as representative populations of odontoprogenitor and osteoprogenitor cells, resp. At first, the present inventors confirmed the differential expression of Alkaline phosphatase (ALP) activity, Dentin matrix protein 1 (DMP 1), Dentin phosphosialoprotein (DSPP) using by real time reverse-transcriptase polymerase chain reaction (RT-PCR) in total RNA from primary cultures. The number of genes in hDPSCs(I) that were up-regulated by 2>-fold, compared to hMSCs, was 614 (Table, IV). On the other band, the number of genes down regulated by <2-fold in hDPSCs (I) was 296 (Table III, IV).

L3 ANSWER 43 OF 58 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN

AN 2006:92025 BIOSIS

DN PREV200600089626

TI Detection of homocysteine and cysteine.

AU Wang, Weihua; Rusin, Oleksandr [Reprint Author]; Xu, Xiangyang; Kim, Kwang; Escobedo, Jorge O.; Fakayode, Sayo O.; Fletcher, Kristin A.; Lowry, Mark; Schowalter, Corin M.; Lawrence, Candace M.; Fronczek, Frank R.; Warner, Isiah M.; Strongin, Robert M.

CS Louisiana State Univ, Dept Chem, Baton Rouge, LA 70803 USA rstrong@lsu.edu

SO Journal of the American Chemical Society, (NOV 16 2005) Vol. 127, No. 45,
pp. 15949-15958.
CODEN: JACSAT. ISSN: 0002-7863.
DT Article
LA English
ED Entered STN: 25 Jan 2006
Last Updated on STN: 25 Jan 2006
AB At elevated levels, homocysteine (Hey, 1) is a risk factor for cardiovascular diseases, Alzheimer's disease, neural tube defects, and osteoporosis. Both 1 and cysteine (Cys, 3) are linked to neurotoxicity. The biochemical mechanisms by which 1 and 3 are involved in disease states are relatively unclear. Herein, we describe simple methods for detecting either Hey or Cys in the visible spectral region with the highest selectivity reported to date without using biochemical techniques or preparative separations. Simple methods and readily available reagents allow for the detection of Cys and Hey in the range of their physiologically relevant levels. New HPLC postcolumn detection methods for biological thiols are reported. The potential biomedical relevance of the chemical mechanisms involved in the detection of 1 is described.

AN 2005456863 EMBASE
TI Hey basic helix-loop-helix transcription factors are repressors of GATA4 and GATA6 and restrict expression of the GATA target gene ANF in fetal hearts.
AU Fischer, Andreas; Klattig, Jurgen; Kneitz, Burkhard; Diez, Holger; Maier, Manfred; Englert, Christoph; Gessler, Manfred (correspondence)
CS Theodor Boveri Institute (Biocenter), Physiological Chemistry I, University of Wuerzburg, Wuerzburg, Germany. gessler@biozentrum.uni-wuerzburg.de
AU Holtmann, Bettina
CS Institut fuer Klinische Neurobiologie, University of Wuerzburg, Wuerzburg, Germany.

AU Gessler, Manfred (correspondence)
CS Theodor-Boveri-Institute, Physiological Chemistry I, Biocenter, University
of Wuerzburg, 97074 Wuerzburg, Germany. gessler@biozentrum.uni-wuerzburg.de
AU Klattig, Jurgen; Englert, Christoph
CS Institute of Molecular Biotechnology, Jena, Germany.
AU Kneitz, Burkhard
CS Urologische Klinik, University of Wuerzburg, Wuerzburg, Germany.
SO Molecular and Cellular Biology, (Oct 2005) Vol. 25, No. 20, pp. 8960-8970.
Refs: 59
ISSN: 0270-7306 CODEN: MCEBD4
CY United States
DT Journal; Article
FS 029 Clinical and Experimental Biochemistry
LA English
SL English
ED Entered STN: 27 Oct 2005
Last Updated on STN: 27 Oct 2005
AB The Hey basic helix-loop-helix transcription factors are downstream
effectors of Notch signaling in the cardiovascular system. Mice lacking
Hey2 develop cardiac hypertrophy, often associated with congenital heart
defects, whereas combined Hey1/Hey2 deficiency leads to severe
vascular defects and embryonic lethality around embryonic day E9.5. The
molecular basis of these disorders is poorly understood, however, since
target genes of Hey transcription factors in the affected tissues remain
elusive. To identify genes regulated by Hey factors we have generated a
conditional Hey1 knockout mouse. This strain was used to
generate paired Hey2- and Hey1/2-deficient embryonic stem cell
lines. Comparison of these cell lines by microarray analysis identified
GATA4 and GATA6 as differentially expressed genes. Loss of Hey1
/2 leads to elevated GATA4/6 and ANF mRNA levels in embryoid bodies, while
forced expression of Hey factors strongly represses expression of the
GATA4 and GATA6 promoter in various cell lines. In addition, the promoter
activity of the GATA4/6 target gene ANF was inhibited by Hey1,
Hey2, and HeyL. Protein interaction and mutation analyses suggest that
repression is due to direct binding of Hey proteins to GATA4 and GATA6,
blocking their transcriptional activity. In Hey2-deficient fetal hearts

we observed elevated mRNA levels of ANF and CARP. Expression of ANF and Hey2 is normally restricted to the trabecular and compact myocardial layer, respectively. Intriguingly, loss of Hey2 leads to ectopic ANF expression in the compact layer, suggesting a direct role for Hey2 in limiting ANF expression in this cardiac compartment. Copyright .COPYRGT. 2005, American Society for Microbiology. All Rights Reserved.

L3 ANSWER 45 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2005:554108 CAPLUS
DN 143:263904
TI Murine T-box transcription factor Tbx20 acts as a repressor during heart development, and is essential for adult heart integrity, function and adaptation
AU Stennard, Fiona A.; Costa, Mauro W.; Lai, Donna; Biben, Christine; Furtado, Milena B.; Solloway, Mark J.; McCulley, David J.; Leimena, Christiana; Preis, Jost I.; Dunwoodie, Sally L.; Elliott, David E.; Prall, Owen W. J.; Black, Brian L.; Fatkin, Diane; Harvey, Richard P.
CS Victor Chang Cardiac Research Institute, St Vincent's Hospital, Darlinghurst, 2010, Australia
SO Development (Cambridge, United Kingdom) (2005), 132(10), 2451-2462
CODEN: DEVPED; ISSN: 0950-1991
PB Company of Biologists Ltd.
DT Journal
LA English
AB The genetic hierarchies guiding lineage specification and morphogenesis of the mammalian embryonic heart are poorly understood. We now show by gene targeting that murine T-box transcription factor Tbx20 plays a central role in these pathways, and has important activities in both cardiac development and adult function. Loss of Tbx20 results in death of embryos at mid-gestation with grossly abnormal heart morphogenesis. Underlying these disturbances was a severely compromised cardiac transcriptional program, defects in the mol. prepattern, reduced expansion of cardiac progenitors and a block to chamber differentiation. Notably, Tbx20-null

embryos showed ectopic activation of Tbx2 across the whole heart myogenic field. Tbx2 encodes a transcriptional repressor normally expressed in non-chamber myocardium, and in the atrioventricular canal it has been proposed to inhibit chamber-specific gene expression through competition with pos. factor Tbx5. Our data demonstrate a repressive activity for Tbx20 and place it upstream of Tbx2 in the cardiac genetic program. Thus, hierarchical, repressive interactions between Tbx20 and other T-box genes and factors underlie the primary lineage split into chamber and non-chamber myocardium in the forming heart, an early event upon which all subsequent morphogenesis depends. Addnl. roles for Tbx20 in adult heart integrity and contractile function were revealed by in-vivo cardiac functional anal. of Tbx20 heterozygous mutant mice. These data suggest that mutations in human cardiac transcription factor genes, possibly including TBX20, underlie both congenital heart disease and adult cardiomyopathies.

RE.CNT 78 THERE ARE 78 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 46 OF 58 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN

AN 2006:181646 BIOSIS

DN PREV200600183758

TI BMP4 induces changes in Jagged 1 expression in bone marrow stroma: Association with induction of Notch regulated genes in CD34+cells.

AU Fagerlie, Sara R. [Reprint Author]; Iwata, Mineo; Graf, Lynn; Torok-Storb, Beverly

CS Fred Hutchinson Canc Res Ctr, Clin Div, Seattle, WA 98104 USA

SO Blood, (NOV 16 2005) Vol. 106, No. 11, Part 1, pp. 401A-402A. Meeting Info.: 47th Annual Meeting of the American-Society-of-Hematology. Atlanta, GA, USA. December 10 -13, 2005. Amer Soc Hematol. CODEN: BLOOAW. ISSN: 0006-4971.

DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)

LA English

ED Entered STN: 15 Mar 2006
Last Updated on STN: 15 Mar 2006

AB In a previous report we identified gene products that may be associated with stein cell maintenance by comparative transcriptome analysis of 2 functionally distinct stromal cell lines: HS-27a which supports primitive hematopoietic progenitor cells and HS-5 which stimulates differentiation. Since the ability of stromal cells to maintain stem cells is lost as the percentage of monocytes in stromal cultures increases, monokine-induced changes in HS-27a gene expression were also determined. An algorithm that combined these datasets was developed and used to identify factors produced by stroma that could be hypothesized to influence hematopoietic stem cell fate. Bone Morphogenetic protein 4 (BMP4) was identified and selected for study. Real time quantitative PCR confirmed that BMP4 gene expression was 9 fold higher in HS-27a than HS-5 and suppressed 6-fold by IL-1 beta. BMP4 protein secretion followed a similar pattern: HS-27a cells secreted 70 pg/ml BMP4 protein and treatment with IL-1 beta resulted in a 3 fold suppression; no BMP-4 secretion was detected from HS-5 cells. BMP4 is a critical factor for regulating hematopoietic development during embryogenesis and is involved in the regulation of T-cell differentiation by thymic stroma. However, relatively little is known about the role of bone marrow stromal derived BMP4 in adult hematopoiesis. BMP4 has been implicated in Notch signaling in muscle development. Since the Notch pathway is a key determinant of stem cell fate in hematopoiesis and the Notch ligand, Jagged 1, is differentially expressed in HS-5 and HS-27a cells, we investigated the effect of BMP4 on stromal expression of Jagged 1. We exposed HS-5 cells to BMP4 and assayed for Jagged I expression by western blot analysis. BMP4 induced both expression and modification of Jagged I in HS-5 cells. To determine if changes in Jagged 1 expression altered signaling between stroma and CD34+ cells, we exposed HS-5 cells to BMP4

for 24 hours, The medium was subsequently removed and replaced with fresh medium that did not contain BMP4. CD34+ cells were then added to the HS-5 cells and incubated at 37 degrees C for 2 to 24 hours. CD34+ cells were collected for RNA extraction and whole cell protein extracts were made from the HS-5 cells to verify changes in Jagged I expression. Pre-incubation of HS-5 cells with BMP4 prior to co-culture, with CD34+ cells resulted in a consistent increase (1.4 to 2.0 fold) in gene expression of the notch regulated genes, Hey1 and Hes1. Although other, as yet undefined, BMP4 induced changes in marrow stroma may be responsible for this induction, we hypothesize that BMP4-induced changes in stromal Jagged 1 expression increases Hey1 and Hes1 gene expression via ligand engagement and activation of Notch signaling. Taken together, these studies suggest that BMP4 acts indirectly on progenitor cells via bone marrow stroma through a previously undescribed mechanism whereby BMP4 induces changes in stromal cell expression of the Notch ligand, Jagged1.

L3 ANSWER 47 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2004:1127487 CAPLUS
DN 142:72870
TI Gene expression profiles in airway epithelium and their use as signatures for diagnosing disorders of the lung
IN Brody, Jerome S.; Spira, Avrum; Shah, Nila; Palma, John F.
PA Trustees of Boston University, USA; Affymetrix, Inc.
SO PCT Int. Appl., 105 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004111197	A2	20041223	WO 2004-US18492	20040610
WO 2004111197	A3	20060720		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,

LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,
SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,
SN, TD, TG

PRAI US 2003-477218P P 20030610
US 2003-483387P P 20030627
US 2003-497599P P 20030825

AB A minimally invasive sample procurement method for obtaining airway epithelial cell RNA that can be analyzed by expression profiling, e.g., by array-based gene expression profiling, is disclosed. These methods can be used to identify patterns of gene expression that are diagnostic of lung disorders, e.g., cancer, to identify subjects at risk for developing lung disorders and to custom design an array, e.g., a microarray, for the diagnosis or prediction of lung disorders or susceptibility to lung disorders. Arrays and informative genes are also disclosed for this purpose.

L3 ANSWER 48 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2004:878503 CAPLUS
DN 141:344623
TI Gene expression profile associated with osteoblast differentiation and osteoporosis diagnosis markers
IN Susa Spring, Mira; Zamurovic, Natasa
PA Novartis A.-G., Switz.; Novartis Pharma G.m.b.H.
SO PCT Int. Appl., 75 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

PI WO 2004090161 A1 20041021 WO 2004-EP3588
20040405
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ,
CA, CH,
CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI,
GB, GD,
GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR,
KZ, LC,
LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ,
NA, NI,
NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK,
SL, SY,
TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA,
ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW,
AM, AZ,
BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE,
DK, EE,
ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO,
SE, SI,
SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR,
NE, SN,
TD, TG
EP 1616026 A1 20060118 EP 2004-725691
20040405
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE,
MC, PT,
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU,
PL, SK, HR
JP 2006523444 T 20061019 JP 2006-504999
20040405
EP 1923401 A2 20080521 EP 2007-119293
20040405
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR,
HU, IE,
IT, LI, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR
US 20070105101 A1 20070510 US 2005-552319
20051018
US 20080118521 A1 20080522 US 2007-924367
20071025
PRAI US 2003-462834P P 20030414
EP 2004-725691 A3 20040405
WO 2004-EP3588 W 20040405
US 2005-552319 A1 20051018
AB He present invention relates to the elucidation of the global
changes in
gene expression during osteoblastic differentiation of MC3T3-E1
cell line, in particular MC3T3-1b clone. In one aspect, the
present
invention relates to detecting a change in an expression level
of one or
more genes or gene families associated with the differentiation
of MC3T3-E1

cells, in particular MC3T3-1 b cells, into osteoblasts. The genes identified may be used as markers for osteoporosis diagnosis or monitoring the treatment of a patient with osteoporosis.

RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 49 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2004:824055 CAPLUS
DN 141:330185
TI Gene expression profiling for diagnosis and treatment of angiogenesis-related disorders
IN Gonda, Thomas John; Kremmidiotis, Gabriel
PA Bionomics Limited, Australia
SO PCT Int. Appl., 148 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2004085675	A1	20041007	WO 2004-AU383	20040326
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1608778	A1	20051228	EP 2004-723453	20040326
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK				

JP 2006524492 T 20061102 JP 2006-503979 20040326
EP 1947199 A2 20080723 EP 2008-5525 20040326
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
IT, LI, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR
US 20060246452 A1 20061102 US 2006-550533 20060428
PRAI AU 2003-901511 A 20030328
EP 2004-723453 A3 20040326
WO 2004-AU383 W 20040326
AB The present invention provides methods of gene expression profiling for diagnosis and treatment of angiogenesis-related disorders. Diseases of the invention include cancer, rheumatoid arthritis, diabetic retinopathy, psoriasis, cardiovascular diseases such as atherosclerosis, ischmeic limb disease and coronary heart disease.
RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 50 OF 58 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN DUPLICATE 12
AN 2004:441310 BIOSIS
DN PREV200400446295
TI Coordinated activation of Notch, Wnt, and transforming growth factor-beta signaling pathways in bone morphogenic protein 2-induced osteogenesis Notch - Target gene Hey1 inhibits mineralization and Runx2 transcriptional activity.
AU Zamurovic, Natasa; Cappellen, David; Rohner, Daisy; Susa, Mira [Reprint Author]
CS Arthrit and Bone Metab Gastrointestinal Dis Area, Novartis Inst Biomed Res, WKL-125-9-12, CH-4002, Basel, Switzerland
mira.susa_spring@pharma.novartis.com
SO Journal of Biological Chemistry, (September 3 2004) Vol. 279, No. 36, pp. 37704-37715. print.
CODEN: JBCHA3. ISSN: 0021-9258.
DT Article
LA English
ED Entered STN: 17 Nov 2004
Last Updated on STN: 17 Nov 2004
AB To examine early events in osteoblast differentiation, we analyzed the expression of about 9,400 genes in the murine MC3T3 cell

line, whose robust differentiation was documented cytochemically and molecularly. The cells were stimulated for 1 and 3 days with the osteogenic stimulus containing bone morphogenic protein 2. Total RNA was extracted and analyzed by Affymetrix GeneChip oligonucleotide arrays. A regulated expression of 394 known genes and 295 expressed sequence tags was detected. The sensitivity and reliability of detection by microarrays was shown by confirming the expression pattern for 20 genes by radioactive quantitative reverse transcription-PCR. Functional classification of regulated genes was performed, defining the groups of regulated growth factors, receptors, and transcription factors. The most interesting finding was concomitant activation of transforming growth factor-beta, Wnt, and Notch signaling pathways, confirmed by strong up-regulation of their target genes by PCR. The transforming growth factor-beta pathway is activated by stimulated production of the growth factor itself, while the exact mechanism of Wnt and Notch activation remains elusive. We showed that bone morphogenic protein 2 stimulated expression of Hey1, a direct Notch target gene, in mouse MC3T3 and C2C12 cells, in human mesenchymal cells, and in mouse calvaria. Small interfering RNA-mediated inhibition of Hey1 induction led to an increase in osteoblast matrix mineralization, suggesting that Hey1 is a negative regulator of osteoblast maturation. This negative regulation is apparently achieved via interaction with Runx2: Hey1 completely abrogated Runx2 transcriptional activity. These findings identify the Notch-Hey1 pathway as a negative regulator of osteoblast differentiation/maturation, which is a completely novel aspect of osteogenesis and could point to possible new targets for bone anabolic agents.

L3 ANSWER 51 OF 58 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN DUPLICATE 13
AN 2004:465277 BIOSIS
DN PREV200400461669
TI Identification of novel regulators associated with early-phase osteoblast differentiation.
AU de Jong, Diana S.; Vaes, Bart L. T.; Dechering, Koen J.; Feijen, Alie;

Hendriks, Jose M. A.; Wehrens, Ron; Mummery, Christine L.; van Zoelen,
Everardus J. J. [Reprint Author]; Olijve, Wiebe; Steegenga, Wilma T.
CS Dept Cell BiolFac FNWI, Univ Nijmegen, Toernooiveld 1, NL-6525 ED,
Nijmegen, Netherlands
vzoelen@sci.kun.nl
SO Journal of Bone and Mineral Research, (June 2004) Vol. 19, No. 6, pp.
947-958. print.
ISSN: 0884-0431 (ISSN print).
DT Article
LA English
ED Entered STN: 1 Dec 2004
Last Updated on STN: 1 Dec 2004
AB Key regulatory components of the BMP-induced osteoblast
differentiation cascade remain to be established. Microarray and
subsequent expression analyses in mice identified two transcription
factors, Hey1 and Tcf7, with in vitro and in vivo expression
characteristics very similar to Cbfa1. Transfection studies suggest that
Tcf7 modulates BMP2-induced osteoblast differentiation. This
study contributes to a better definition of the onset of BMP-induced
osteoblast differentiation.

L3 ANSWER 52 OF 58 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on
STN
AN 2005:395802 BIOSIS
DN PREV200510185834
TI Hey1, a direct Notch target gene, is up-regulated by BMP-2 and
reduces osteoblast matrix mineralization and Cbfa1/Runx2
transcriptional activity.
AU Susa, Mira [Reprint Author]; Zamurovic, Natasa; Cappellen, David; Rohner,
Daisy
CS Novartis Inst Biomed Res, Basel, Switzerland
SO FASEB Journal, (MAY 14 2004) Vol. 18, No. 8, Suppl. S, pp. C158.
Meeting Info.: Annual Meeting of the American-Society-for-Biochemistry-and-
Molecular-Biology/8th Congress of the International-Union-for-Biochemistry-
and-Molecular-Biology. Boston, MA, USA. June 12 -16, 2004. Amer Soc
BioChem & Mol Biol; Int Union Biochem & Mol Biol.
CODEN: FAJOEC. ISSN: 0892-6638.
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LA English

ED Entered STN: 5 Oct 2005
Last Updated on STN: 5 Oct 2005
AB To examine early events in osteoblast differentiation, we analyzed the expression of about 9,400 genes in the murine MC3T3 cell line, whose robust differentiation was documented cytochemically and molecularly. The cells were stimulated for I and 3 days with the osteogenic stimulus containing bone morphogenetic protein 2 (BMP-2). Total RNA was extracted and analyzed by Affymetrix GeneChipoligonucleotide arrays. A regulated expression of 3 94 known genes and 295 expressed sequence tags (EST) was detected. The sensitivity and reliability of detection by microarrays was shown by confirming the expression pattern for 20 genes by radioactive quantitative RT-PCR.
Functional classification of regulated genes was performed, defining the groups of regulated Growth Factors, Receptors and Transcription Factors.
The most interesting finding was concomitant activation of TGF-beta, Writ and Notch signaling pathways, confirmed by strong up-regulation of their target genes by PCR. TGF-beta pathway is activated by stimulated production of the growth factor itself, while mechanism of Writ and Notch activation remains elusive. We showed BMP-2 stimulated expression of Hey1, a direct Notch target gene, in mouse C2C12 cells, human mesenchymal cells and mouse calvaria. SiRNA-mediated inhibition of Hey1 induction led to an increase in osteoblast matrix mineralization, suggesting that Hey1 is a negative regulator of osteoblast maturation. This negative regulation is apparently achieved via interaction with Cbfa1/Runx2: Hey1 completely abrogated Cbfa1/Runx2 transcriptional activity. These findings identify Notch-Hey1 pathway as a negative regulator of osteoblast differentiation/maturation, which is a completely novel aspect of osteogenesis.

L3 ANSWER 53 OF 58 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN DUPLICATE 14
AN 2004:349102 BIOSIS
DN PREV200400350335
TI Regulation of Notch signaling genes during BMP2-induced differentiation of

osteoblast precursor cells.
AU de Jong, D. S.; Steegenga, W. T.; Hendriks, J. M. A.; Van Zoelen, E. J. J.
[Reprint Author]; Olijve, W.; Dechering, K. J.
CS Dept Cell Biol, Radboud Univ, Nijmegen, Netherlands
vzoelen@sei.kun.nl
SO Biochemical and Biophysical Research Communications, (July 16 2004) Vol.
320, No. 1, pp. 100-107. print.
CODEN: BBRCA9. ISSN: 0006-291X.
DT Article
LA English
ED Entered STN: 18 Aug 2004
Last Updated on STN: 18 Aug 2004
AB The bone morphogenetic protein (BMP)-induced Smad signal transduction pathway is an important positive regulator of osteoblast differentiation. BMP and other members of the transforming growth factor-beta (TGF-beta) family have distinct effects on osteoblast differentiation, depending on cell type and cell differentiation status. In C2C12 mesenchymal cells, BMP-induced osteoblast differentiation can be blocked by TGF-beta. In a search for key regulators of osteoblast differentiation we have used microarray analysis to identify genes which are differentially regulated by BMP2 and TGF-beta. Within the first 24 h following the onset of differentiation, 61 BMP2-regulated genes were identified of which the BMP2 effect was counteracted by TGF-beta. The majority of these differentially expressed transcripts are related to signal transduction. Notably, our data show that three Notch signal transduction pathway genes, Lfng, Hey1, and Hes1, are differentially regulated by BMP2 and TGF-beta. This suggests that these genes might function as the focal point for interaction of Smad and Notch signaling during osteoblast differentiation.

L3 ANSWER 54 OF 58 BIOSIS DUPLICATE 15
AN 2004:47443 BIOSIS
DN PREV200400040106
TI Functional Notch signaling is required for BMP4-induced inhibition of myogenic differentiation.
AU Dahlqvist, Camilla; Blokzijl, Andries; Chapman, Gavin; Falk, Anna; Dannaeus, Karin; Ibanez, Carlos F.; Lendahl, Urban [Reprint Author]

CS Department of Cell and Molecular Biology, Karolinska Institute, SE-171 77,
Stockholm, Sweden
Urban.Lendahl@cmb.ki.se
SO Development (Cambridge), (December 2003) Vol. 130, No. 24, pp. 6089-6099.
print.
CODEN: DEVPED. ISSN: 0950-1991.
DT Article
LA English
ED Entered STN: 14 Jan 2004
Last Updated on STN: 14 Jan 2004
AB The bone morphogenetic protein (BMP) and Notch signaling pathways are crucial for cellular differentiation. In many cases, the two pathways act similarly; for example, to inhibit myogenic differentiation.
It is not known whether this inhibition is caused by distinct mechanisms or by an interplay between Notch and BMP signaling. Here we demonstrate that functional Notch signaling is required for BMP4-mediated block of differentiation of muscle stem cells, i.e. satellite cells and the myogenic cell line C2C12. Addition of BMP4 during induction of differentiation dramatically reduced the number of differentiated satellite and C2C12 cells. Differentiation was substantially restored in BMP4-treated cultures by blocking Notch signaling using either the gamma-secretase inhibitor L-685,458 or by introduction of a dominant-negative version of the Notch signal mediator CSL. BMP4 addition to C2C12 cells increased transcription of two immediate Notch responsive genes, Hes1 and Hey1, an effect that was abrogated by L-685,458. A 3 kb Hey1-promoter reporter construct was synergistically activated by the Notch 1 intracellular domain (Notch 1 ICD) and BMP4. The BMP4 mediator SMAD1 mimicked BMP activation of the Hey1 promoter. A synthetic Notch-responsive promoter containing no SMAD1 binding sites responded to SMAD1, indicating that DNA-binding activity of SMAD1 is not required for activation. Accordingly, Notch 1 ICD and SMAD1 interacted in binding experiments in vitro. Thus, the data presented here provide evidence for a direct interaction between the Notch and BMP signaling pathways, and indicate that Notch has a crucial role in the

execution of certain aspects of BMP-mediated differentiation control.

L3 ANSWER 55 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2002:391917 CAPLUS
DN 136:398177
TI Profiling tumor specific markers for the diagnosis and treatment of
neoplastic disease
IN Palm, Kaia
PA Cemines, LLC, USA
SO PCT Int. Appl., 41 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002040716	A2	20020523	WO 2001-US43461	20011113
WO 2002040716	A3	20030515		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2432639	A1	20020523	CA 2001-2432639	20011113
AU 2002026912	A	20020527	AU 2002-26912	20011113
US 20030092009	A1	20030515	US 2001-992665	20011113
EP 1337667	A2	20030827	EP 2001-995862	20011113
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
US 20070161023	A1	20070712	US 2006-606786	20061130

PRAI US 2000-249508P P 20001116
US 2001-992665 B1 20011113
WO 2001-US43461 W 20011113
AB A method of diagnosing cancer comprising the identification of neoplastic
mol. markers is disclosed. Tumor-related or neoplastic mol. markers are
identified from samples taken from a subject and the mol. profile of those
markers is determined Based upon the neoplastic mol. marker profile of the
subject, the tumor sub-type is ascertained and an appropriate treatment
protocol initiated. The markers are analyzed by immunoassay or the
quantity of RNA or DNA encoding the markers is determined A profile was made
of autoantibodies against transcription factors in the blood of subjects
with prostate cancer using blotted peptides of the transcription factors.

L3 ANSWER 56 OF 58 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on
STN DUPLICATE 16
AN 2002:497600 BIOSIS
DN PREV200200497600
TI Axial skeletal defects caused by mutation in the spondylocostal
dysplasia/pudgy gene Dll3 are associated with disruption of the
segmentation clock within the presomitic mesoderm.
AU Dunwoodie, Sally L. [Reprint author]; Clements, Melanie; Sparrow, Duncan
B.; Sa, Xin; Conlon, Ronald A.; Beddington, Rosa S. P.
CS Division of Mammalian Development, National Institute for Medical
Research, The Ridgeway, Mill Hill, London, NW7 1AA, UK
s.dunwoodie@victorchang.unsw.edu.au
SO Development (Cambridge), (April, 2002) Vol. 129, No. 7, pp. 1795-1806.
print.
CODEN: DEVPED. ISSN: 0950-1991.
DT Article
LA English
ED Entered STN: 25 Sep 2002
Last Updated on STN: 25 Sep 2002
AB A loss-of-function mutation in the mouse delta-like3 (Dll3) gene has been
generated following gene targeting, and results in severe axial skeletal
defects. These defects, which consist of highly disorganised vertebrae
and costal defects, are similar to those associated with the
Dll3-dependent pudgy mutant in mouse and with spondylocostal dysplasia

(MIM 277300) in humans. This study demonstrates that Dll3neo and Dll3pu are functionally equivalent alleles with respect to the skeletal dysplasia, and we suggest that the three human DLL3 mutations associated with spondylocostal dysplasia are also functionally equivalent to the Dll3neo null allele. Our phenotypic analysis of Dll3neo/Dll3neo mutants shows that the developmental origins of the skeletal defects lie in delayed and irregular somite formation, which results in the perturbation of anteroposterior somite polarity. As the expression of Lfng, Hes1, Hes5 and Hey1 is disrupted in the presomitic mesoderm, we suggest that the somitic aberrations are founded in the disruption of the segmentation clock that intrinsically oscillates within presomitic mesoderm.

L3 ANSWER 57 OF 58 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
AN 2002:487459 BIOSIS
DN PREV200200487459
TI BMP regulation of stem cell differentiation.
AU Kessler, J. A. [Reprint author]; Gomes, W. [Reprint author]; Guha, U. [Reprint author]; Israsena, N. [Reprint author]
CS Department of Neurology, Medical School, North-Western University, Chicago, IL, 60611, USA
SO Journal of Neurochemistry, (June, 2002) Vol. 81, No. Supplement 1, pp. 1. print.
Meeting Info.: Thirty-Third Annual Meeting of the American Society for Neurochemistry. Palm Beach, Florida, USA. June 22-26, 2002.
CODEN: JONRA9. ISSN: 0022-3042.
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LA English
ED Entered STN: 18 Sep 2002
Last Updated on STN: 18 Sep 2002

L3 ANSWER 58 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2001:187083 CAPLUS
DN 135:283870
TI E2Fs regulate the expression of genes involved in differentiation, development, proliferation, and apoptosis

AU Muller, Heiko; Bracken, Adrian P.; Vernell, Richard; Moroni, M. Cristina;
Christians, Fred; Grassilli, Emanuela; Prosperini, Elena; Vigo, Elena;
Oliner, Jonathan D.; Helin, Kristian
CS Department of Experimental Oncology, European Institute of Oncology,
Milan, 20141, Italy
SO Genes & Development (2001), 15(3), 267-285
CODEN: GEDEEP; ISSN: 0890-9369
PB Cold Spring Harbor Laboratory Press
DT Journal
LA English
AB The retinoblastoma protein (pRB) and its two relatives, p107 and p130,
regulate development and cell proliferation in part by inhibiting the
activity of E2F-regulated promoters. High-d. oligonucleotide arrays were
used to identify genes in which expression changed in response to
activation of E2F1, E2F2, and E2F3. The E2Fs control the expression of
several genes that are involved in cell proliferation. The E2Fs also
regulate a number of genes involved in apoptosis, differentiation, and
development. These results provide possible genetic explanations to the
variety of phenotypes observed as a consequence of a deregulated pRB/E2F
pathway.
RE.CNT 61 THERE ARE 61 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> FIL STNGUIDE

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	173.00	173.21

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-22.40	-22.40

FILE 'STNGUIDE' ENTERED AT 15:06:16 ON 12 AUG 2008

FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: Aug 8, 2008 (20080808/UP).

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=>
=> FIL BIOSIS CAPLUS EMBASE
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                         ENTRY    SESSION
FULL ESTIMATED COST                                       2.10     175.31

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
                                                         ENTRY    SESSION
CA SUBSCRIBER PRICE                                       0.00
-22.40

FILE 'BIOSIS' ENTERED AT 15:26:59 ON 12 AUG 2008
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FILE 'EMBASE' ENTERED AT 15:26:59 ON 12 AUG 2008
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=> s MC3T3
L4        6460 MC3T3

=> d his

     (FILE 'HOME' ENTERED AT 15:00:59 ON 12 AUG 2008)

     FILE 'BIOSIS, CAPLUS, EMBASE' ENTERED AT 15:01:13 ON 12 AUG 2008
L1          299 S HEY1 OR HEY 1
L2           83 S L1 AND (BONE OR OSTEO?)
L3           58 DUP REM L2 (25 DUPLICATES REMOVED)

     FILE 'STNGUIDE' ENTERED AT 15:06:16 ON 12 AUG 2008

     FILE 'BIOSIS, CAPLUS, EMBASE' ENTERED AT 15:26:59 ON 12 AUG 2008
L4         6460 S MC3T3

=> s l1 and l4
L5          10 L1 AND L4

=> dup rem l5
PROCESSING COMPLETED FOR L5
L6            6 DUP REM L5 (4 DUPLICATES REMOVED)

=> d bib abs 1-
YOU HAVE REQUESTED DATA FROM 6 ANSWERS - CONTINUE? Y/(N):y

L6   ANSWER 1 OF 6  BIOSIS  COPYRIGHT (c) 2008 The Thomson
Corporation  on STN
     DUPLICATE 1
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AN 2007:203797 BIOSIS
DN PREV200700196794
TI CCN3/NOV inhibits BMP-2-induced osteoblast differentiation by interacting
with BMP and Notch signaling pathways.
AU Minamizato, Tokutaro; Sakamoto, Kei; Liu, Tingjiao; Kokubo, Hiroki;
Katsube, Ken-ichi; Perbal, Bernard; Nakamura, Seiji; Yamaguchi, Akira
[Reprint Author]
CS Tokyo Med and Dent Univ, Grad Sch, Sect Oral Pathol, Bunkyo Ku, 1-5-45
Yushima, Tokyo 1138549, Japan
akira.mpa@tmd.ac.jp
SO Biochemical and Biophysical Research Communications, (MAR 9 2007) Vol.
354, No. 2, pp. 567-573.
CODEN: BBRCA9. ISSN: 0006-291X.
DT Article
LA English
ED Entered STN: 21 Mar 2007
Last Updated on STN: 21 Mar 2007
AB We elucidate the role of CCN3/NOV, a member of the CCN family proteins, in
osteoblast differentiation using MC3T3-E1 osteoblastic cells.
Transduction with CCN3 adenovirus (AdCCN3) alone induced no apparent
changes in the expression of osteoblast-related markers, whereas
cotransduction with BMP-2 adenovirus (AdBMP-2) and AdCCN3 significantly
inhibited the AdBMP-2-induced mRNA expression of Runx2, osterix, ALP, and
osteocalcin. Immunoprecipitation-western analysis revealed that CCN3
associated with BMP-2. Compared to transduction with AdBMP-2 alone,
cotransduction with AdBMP-2 and AdCCN3 attenuated the expression of
phosphorylated Smad1/5/8 and the mRNA for Id1, M2, and M3. Transduction
with AdCCN3 stimulated the expression of cleaved Notch1, the mRNA
expression of Hes1 and Hey1/Hesr1, and the promoter activities
of Hes1 and Hey1. The inhibitory effects of CCN3 on the
expression of BMP-2-induced osteoblast-related markers were nullified in
Hey1-deficient osteoblastic cells. These results indicate that
CCN3 exerts inhibitory effects on BMP-2-induced osteoblast differentiation
by its involvement of the BMP and Notch signaling pathways.

L6 ANSWER 2 OF 6 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
AN 2008:214147 BIOSIS
DN PREV200800225906
TI CCN3/NOV inhibits BMP-2-induced osteoblast differentiation by interacting
with BMP and notch signaling pathways.
AU Minamizato, T. [Reprint Author]; Sakamoto, K.; Nakamura, S.; Yamaguchi, A.
CS Tokyo Med and Dent Univ, Grad Sch, Sect Oral Pathol, Tokyo, Japan
SO Journal of Bone and Mineral Research, (SEP 2007) Vol. 22, No. Suppl. 1,
pp. S249.
Meeting Info.: 29th Annual Meeting of the American-Society-for-Bone-and-
Mineral-Research. Honolulu, HI, USA. September 16 -19, 2007. Amer Soc Bone
& Mineral Res.
CODEN: JBMREJ. ISSN: 0884-0431.
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LA English
ED Entered STN: 26 Mar 2008
Last Updated on STN: 26 Mar 2008

L6 ANSWER 3 OF 6 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
AN 2007:98064 BIOSIS
DN PREV200700103571
TI BMP-2 induces Hey1 and HES1 in osteoblastic cells via
Notch-dependent and - Independent signaling pathways.
AU Vukcevic, M. [Reprint Author]; Zamurovic, N.; Luong-Nguyen, N.; Geffers,
I.; Gossler, A.; Susa, M.
CS Novartis Inst BioMed Res, Basel, Switzerland
SO Journal of Bone and Mineral Research, (SEP 2006) Vol. 21, No. Suppl. 1,
pp. S384.
Meeting Info.: 28th Annual Meeting of the American-Society-for-Bone-and-
Mineral-Research. Philadelphia, PA, USA. September 15 -19, 2006. Amer Soc
Bone & Mineral Res.
CODEN: JBMREJ. ISSN: 0884-0431.
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LA English
ED Entered STN: 7 Feb 2007
Last Updated on STN: 7 Feb 2007

L6 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2004:878503 CAPLUS

DN 141:344623
TI Gene expression profile associated with osteoblast differentiation and
osteoporosis diagnosis markers
IN Susa Spring, Mira; Zamurovic, Natasa
PA Novartis A.-G., Switz.; Novartis Pharma G.m.b.H.
SO PCT Int. Appl., 75 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004090161	A1	20041021	WO 2004-EP3588	20040405
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1616026	A1	20060118	EP 2004-725691	20040405
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR				
JP 2006523444	T	20061019	JP 2006-504999	20040405
EP 1923401	A2	20080521	EP 2007-119293	20040405
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LI, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR				
US 20070105101	A1	20070510	US 2005-552319	20051018

US 20080118521 A1 20080522 US 2007-924367
20071025
PRAI US 2003-462834P P 20030414
EP 2004-725691 A3 20040405
WO 2004-EP3588 W 20040405
US 2005-552319 A1 20051018
AB He present invention relates to the elucidation of the global changes in
gene expression during osteoblastic differentiation of MC3T3-E1 cell line, in particular MC3T3-1b clone. In one aspect, the present invention relates to detecting a change in an expression level of
one or more genes or gene families associated with the differentiation of
MC3T3-E1 cells, in particular MC3T3-1 b cells, into osteoblasts. The genes identified may be used as markers for osteoporosis
diagnosis or monitoring the treatment of a patient with osteoporosis.
RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 5 OF 6 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
DUPLICATE 2
AN 2004:441310 BIOSIS
DN PREV200400446295
TI Coordinated activation of Notch, Wnt, and transforming growth factor-beta
signaling pathways in bone morphogenic protein 2-induced osteogenesis
Notch - Target gene Hey1 inhibits mineralization and Runx2 transcriptional activity.
AU Zamurovic, Natasa; Cappellen, David; Rohner, Daisy; Susa, Mira [Reprint
Author]
CS Arthrit and Bone Metab Gastrointestinal Dis Area, Novartis Inst Biomed
Res, WKL-125-9-12, CH-4002, Basel, Switzerland
mira.susa_spring@pharma.novartis.com
SO Journal of Biological Chemistry, (September 3 2004) Vol. 279, No. 36, pp.
37704-37715. print.
CODEN: JBCHA3. ISSN: 0021-9258.
DT Article
LA English
ED Entered STN: 17 Nov 2004
Last Updated on STN: 17 Nov 2004
AB To examine early events in osteoblast differentiation, we analyzed the
expression of about 9,400 genes in the murine MC3T3 cell line, whose robust differentiation was documented cytochemically and

molecularly. The cells were stimulated for 1 and 3 days with the osteogenic stimulus containing bone morphogenic protein 2. Total RNA was extracted and analyzed by Affymetrix GeneChip oligonucleotide arrays. A regulated expression of 394 known genes and 295 expressed sequence tags was detected. The sensitivity and reliability of detection by microarrays was shown by confirming the expression pattern for 20 genes by radioactive quantitative reverse transcription-PCR. Functional classification of regulated genes was performed, defining the groups of regulated growth factors, receptors, and transcription factors. The most interesting finding was concomitant activation of transforming growth factor-beta, Wnt, and Notch signaling pathways, confirmed by strong up-regulation of their target genes by PCR. The transforming growth factor-beta pathway is activated by stimulated production of the growth factor itself, while the exact mechanism of Wnt and Notch activation remains elusive. We showed that bone morphogenic protein 2 stimulated expression of Hey1, a direct Notch target gene, in mouse MC3T3 and C2C12 cells, in human mesenchymal cells, and in mouse calvaria. Small interfering RNA-mediated inhibition of Hey1 induction led to an increase in osteoblast matrix mineralization, suggesting that Hey1 is a negative regulator of osteoblast maturation. This negative regulation is apparently achieved via interaction with Runx2: Hey1 completely abrogated Runx2 transcriptional activity. These findings identify the Notch-Hey1 pathway as a negative regulator of osteoblast differentiation/maturation, which is a completely novel aspect of osteogenesis and could point to possible new targets for bone anabolic agents.

L6 ANSWER 6 OF 6 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
AN 2005:395802 BIOSIS
DN PREV200510185834
TI Hey1, a direct Notch target gene, is up-regulated by BMP-2 and reduces osteoblast matrix mineralization and Cbfa1/Runx2 transcriptional activity.

AU Susa, Mira [Reprint Author]; Zamurovic, Natasa; Cappellen, David; Rohner, Daisy
CS Novartis Inst Biomed Res, Basel, Switzerland
SO FASEB Journal, (MAY 14 2004) Vol. 18, No. 8, Suppl. S, pp. C158. Meeting Info.: Annual Meeting of the American-Society-for-Biochemistry-and-Molecular-Biology/8th Congress of the International-Union-for-Biochemistry-and-Molecular-Biology. Boston, MA, USA. June 12 -16, 2004. Amer Soc BioChem & Mol Biol; Int Union Biochem & Mol Biol.
CODEN: FAJOEC. ISSN: 0892-6638.
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LA English
ED Entered STN: 5 Oct 2005
Last Updated on STN: 5 Oct 2005
AB To examine early events in osteoblast differentiation, we analyzed the expression of about 9,400 genes in the murine MC3T3 cell line, whose robust differentiation was documented cytochemically and molecularly. The cells were stimulated for I and 3 days with the osteogenic stimulus containing bone morphogenetic protein 2 (BMP-2).
Total RNA was extracted and analyzed by Affymetrix GeneChipoligonucleotide arrays. A regulated expression of 3 94 known genes and 295 expressed sequence tags (EST) was detected. The sensitivity and reliability of detection by microarrays was shown by confirming the expression pattern for 20 genes by radioactive quantitative RT-PCR. Functional classification of regulated genes was performed, defining the groups of regulated Growth Factors, Receptors and Transcription Factors. The most interesting finding was concomitant activation of TGF-beta, Writ and Notch signaling pathways, confirmed by strong up-regulation of their target genes by PCR. TGF-beta pathway is activated by stimulated production of the growth factor itself, while mechanism of Writ and Notch activation remains elusive. We showed BMP-2 stimulated expression of Hey1, a direct Notch target gene, in mouse C2C12 cells, human mesenchymal cells and mouse calvaria. SiRNA-mediated inhibition of Hey1 induction led to an increase in osteoblast matrix mineralization, suggesting that

Hey1 is a negative regulator of osteoblast maturation. This negative regulation is apparently achieved via interaction with Cbfa1/Runx2: Hey1 completely abrogated Cbfa1/Runx2 transcriptional activity. These findings identify Notch-Hey1 pathway as a negative regulator of osteoblast differentiation/maturation, which is a completely novel aspect of osteogenesis.

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=> FIL STNGUIDE
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
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FULL ESTIMATED COST                                      19.14     194.45

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
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CA SUBSCRIBER PRICE                                      -0.80
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     (FILE 'HOME' ENTERED AT 15:00:59 ON 12 AUG 2008)

     FILE 'BIOSIS, CAPLUS, EMBASE' ENTERED AT 15:01:13 ON 12 AUG 2008
L1           299 S HEY1 OR HEY 1
L2            83 S L1 AND (BONE OR OSTEO?)
L3            58 DUP REM L2 (25 DUPLICATES REMOVED)

     FILE 'STNGUIDE' ENTERED AT 15:06:16 ON 12 AUG 2008

     FILE 'BIOSIS, CAPLUS, EMBASE' ENTERED AT 15:26:59 ON 12 AUG 2008
L4          6460 S MC3T3
L5            10 S L1 AND L4
L6             6 DUP REM L5 (4 DUPLICATES REMOVED)

     FILE 'STNGUIDE' ENTERED AT 15:28:47 ON 12 AUG 2008

=> FIL BIOSIS CAPLUS EMBASE
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                         ENTRY    SESSION
FULL ESTIMATED COST                                       2.58     197.03

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
                                                         ENTRY    SESSION
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=> s osteoporosis
L7 101608 OSTEOPOROSIS

=> s l7 and review
L8 19296 L7 AND REVIEW

=> d bib abs 1-10

L8 ANSWER 1 OF 19296 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on
STN
AN 2008:427848 BIOSIS
DN PREV200800427847
TI Incidence and prevalence of medication-induced osteoporosis: evidence-based review.
AU Allport, Juliette [Reprint Author]
CS Wolters Kluwer Hlth Adis, Auckland, New Zealand
SO Current Opinion in Rheumatology, (JUL 2008) Vol. 20, No. 4, pp. 435-441.
ISSN: 1040-8711.
DT Article
General Review; (Literature Review)
LA English
ED Entered STN: 6 Aug 2008
Last Updated on STN: 6 Aug 2008
AB (1) While a number of medications have been shown to induce bone loss, the actual incidence and prevalence of medication-induced osteoporosis has not been well quantified.(2) Oral corticosteroids contribute to an increased prevalence of osteoporosis and an increased incidence of fracture in a number of different populations. The increased incidence of fracture in patients receiving inhaled corticosteroids for respiratory disease may be attributed to disease pathogenesis rather than the effects

of medication.(3) Other therapies that increase the incidence and/or prevalence of medication induced osteoporosis and fracture include androgen-deprivation therapy, aromatase inhibitors, protease inhibitors, selective serotonin reuptake inhibitors and prolactin-raising antiepileptic agents.(4) It is difficult to make definitive conclusions on the actual increase in the prevalence and/or incidence of osteoporosis in patients receiving certain medications, as values are often reported differently and studies are mainly retrospective and are therefore open to inherent selection biases and other confounders. Furthermore, there is little available information as to whether specific medications within a class are associated with a higher rate of bone disease than others.

L8 ANSWER 2 OF 19296 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
AN 2008:427847 BIOSIS
DN PREV200800427846
TI Bone and fat connection in aging bone.
AU Duque, Gustavo [Reprint Author]
CS Nepean Hosp, Nepean Clin Sch, Level 5,South Block, Penrith, NSW 2750, Australia
gduque@med.usyd.edu.au
SO Current Opinion in Rheumatology, (JUL 2008) Vol. 20, No. 4, pp. 429-434.
ISSN: 1040-8711.
DT Article
General Review; (Literature Review)
LA English
ED Entered STN: 6 Aug 2008
Last Updated on STN: 6 Aug 2008
AB Purpose of review The fat and bone connection plays an important role in the pathophysiology of age-related bone loss. This review will focus on the age-induced mechanisms regulating the predominant differentiation of mesenchymal stem cells into adipocytes. Additionally, bone marrow fat will be considered as a diagnostic and therapeutic approach to osteoporosis.Recent findings There are two types of bone and fat connection. The'systemic connection', usually seen in obese

patients, is hormonally regulated and associated with high bone mass and strength. The'local connection' happens inside the bone marrow. Increasing amounts of bone marrow fat affect bone turnover through the inhibition of osteoblast function and survival and the promotion of osteoclast differentiation and activation. This interaction is regulated by paracrine secretion of fatty acids and adipokines. Additionally, bone marrow fat could be quantified using noninvasive methods and could be used as a therapeutic approach due to its capacity to transdifferentiate into bone without affecting other types of fat in the body.Summary The bone and fat connection within the bone marrow constitutes a typical example of lipotoxicity. Additionally, bone marrow fat could be used as a new diagnostic and therapeutic approach for osteoporosis in older persons.

L8 ANSWER 3 OF 19296 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
AN 2008:427846 BIOSIS
DN PREV200800427845
TI Male osteoporosis: new insights in an understudied disease.
AU Haney, Elizabeth M. [Reprint Author]; Bliziotes, M. Michael
CS Oregon Hlth and Sci Univ, Div Gen Internal Med, Dept Med, 3181 SW Sam Jackson Ark Rd,L-475, Portland, OR 97239 USA haneye@ohsu.edu
SO Current Opinion in Rheumatology, (JUL 2008) Vol. 20, No. 4, pp. 423-428. ISSN: 1040-8711.
DT Article General Review; (Literature Review)
LA English
ED Entered STN: 6 Aug 2008 Last Updated on STN: 6 Aug 2008
AB Purpose of review Osteoporosis in men is increasingly recognized as an important health problem. New research contributes to our knowledge of gender differences in osteoporosis risk, diagnosis and management. We undertook this review to summarize recent developments in the field of male osteoporosis.Recent findings The paper reviews recently published studies that reveal new insights into male osteoporosis. It addresses epidemiology,

risk factors, use of clinical risk assessment tools, diagnosis and treatment. New data continue to suggest that men have higher mortality rates than women after hip fracture, and that men may experience fractures at higher bone mineral density values than women. Treatments for osteoporosis have been studied mostly in women, but trials including both men and women are now being conducted. Likewise, there are several newer cohorts with bone and fracture outcomes that include men and women. The Osteoporotic Fractures in Men (MrOS) study is the first United States-based cohort to include only men; this study is contributing importantly to our understanding of epidemiology and risk factors for osteoporosis in men.Summary Men and their physicians should be aware of the risk for osteoporosis and the gender differences that exist within this disease. Further research is needed to continue to understand differences in pathophysiology, epidemiology and risk factors, and to promote appropriate therapies among men.

L8 ANSWER 4 OF 19296 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
AN 2008:425959 BIOSIS
DN PREV200800425958
TI Utility values associated with osteoporotic fracture: A systematic review of the literature.
AU Hiligsmann, Mickael [Reprint Author]; Ethgen, Olivier; Richy, Florent; Reginster, Jean-Yves
CS Univ Liege, Dept Epidemiol Publ Hlth and Hlth Econ, Ave Hosp,Bat B23, B-4000 Liege, Belgium
m.hiligsmann@ulg.ac.be
SO Calcified Tissue International, (APR 2008) Vol. 82, No. 4, pp. 288-292.
CODEN: CTINDZ. ISSN: 0171-967X.
DT Article
General Review; (Literature Review)
LA English
ED Entered STN: 6 Aug 2008
Last Updated on STN: 6 Aug 2008
AB We reviewed studies that have estimated the impact of osteoporotic fracture on quality-adjusted life years (QALY) and to determine reference

values for countries that would like to carry out cost-utility analyses but that do not have their own values. The computerized medical literature databases Medline and EMBASE were searched from January 1990 to December 2006. The search was carried out in two steps. The first step was to identify studies that related to quality of life in osteoporosis. As part of the second step, only the studies that translated quality of life into a utility value (one single value for health status ranging 0 - 1) and calculated a utility loss over a period of at least 1 year were selected. From the 152 studies identified in the first analysis, only 16 were retained after the second step. Ten studies investigated utility values for hip fractures, 11 for vertebral fractures, five for distal forearm fractures, and four for other osteoporotic fractures and fracture interactions. Utility values differed substantially between studies, partly due to the valuation technique used, the severity of fractures, and the sample size. This review suggests that there is no meaningful average value across different studies, different samples, different countries, or different instruments. Although we tried to determine the best available values, these values do not preclude the need for country-specific studies. Finally, we also make recommendations regarding the design and methodology for such studies.

L8 ANSWER 5 OF 19296 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN

AN 2008:424978 BIOSIS

DN PREV200800424977

TI Recommandations for the management of bone demineralization in cystic fibrosis.
Original Title: Recommandations pour la prise en charge de la demineralisation osseuse dans la mucoviscidose.

AU Sermet-Gaudelus, I. [Reprint Author]; Nove-Josserand, R.; Loeille, G. -A.; Dacremont, G.; Souberbielle, J. -C.; Fritsch, J.; Laurans, M.; Moulin, P.; Cortet, B.; Salles, J. -P.; Ginies, J. -L.; Guillot, M.; Perez-Martin, S.;

Ruiz, J. -C.; Montagne, V.; Cohen-Solal, M.; Cormier, C.; Garabedian, M.;
Mallet, E.
CS Hop Necker Enfants Malad, CRCM Necker Enfants Malad, 149,Rue Serv, F-75015
Paris, France
isabelle.sermet@nck.aphp.fr
SO Archives de Pediatrie, (MAR 2008) Vol. 15, No. 3, pp. 301-312.
ISSN: 0929-693X.
DT Article
General Review; (Literature Review)
LA French
ED Entered STN: 6 Aug 2008
Last Updated on STN: 6 Aug 2008
AB A high prevalence of low bone mineralization is documented in adult
patients with cystic fibrosis (CF). Osteopenia is present in as much as
85% of adult patients and osteoporosis in 13 to 57% of them. In
children, studies are discordant probably because of different control
database. Denutrition, inflammation, vitamin D and vitamin K deficiency,
altered sex hormone production, glucocorticoid therapy, and physical
inactivity are well known risk factors for poor bone health. Puberty is a
critical period and requires a careful follow-up for an optimal bone peak
mass. This review is a consensus statement established by the
national working group of the French Federation of CF Centers to develop
practice guidelines for optimizing bone health in patients with CF.
Recommendations for screening and for calcium, vitamin D and K
supplementation are given. Further work is needed to define indications
for treatment with biphosphonates and anabolic agents.

L8 ANSWER 6 OF 19296 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on
STN
AN 2008:424246 BIOSIS
DN PREV200800424245
TI Hormone-dependent aging problems in women.
AU Jung, Byung Hwa; Jeon, Myting Jae; Bai, Sang Wook [Reprint Author]
CS Yonsei Univ, Dept Obstet and Gynecol, Coll Med, 250 Seongsanno, Seoul
120752, South Korea

swbai@yuhs.ac
SO Yonsei Medical Journal, (JUN 30 2008) Vol. 49, No. 3, pp. 345-351.
CODEN: YOMJA9. ISSN: 0513-5796.
DT Article
General Review; (Literature Review)
LA English
ED Entered STN: 31 Jul 2008
Last Updated on STN: 31 Jul 2008
AB One of the major social issues nowadays is the aging society. Korea is already an aging society, and 63 cities and districts are ultra-aged societies where the rate of people older than 65 yr exceeds 20%. Among them, more than 67% are women. These statistics reveal the importance of healthcare for older women. Disease and disability of older women are very closely related to the loss of female sex hormones after menopause. Major hormone-dependent aging problems in women such as osteoporosis, Alzheimer's disease (AD), urinary incontinence, and coronary atherosclerosis were surveyed in this review, and the key role of hormones in those diseases and hormone replacement therapy (HRT) were summarized. We expect that this review would provide some understanding of factors that must be considered to give optimal care to older women for healthy lives.

L8 ANSWER 7 OF 19296 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
AN 2008:424214 BIOSIS
DN PREV200800424213
TI Imagination and creation: 1-hydroxyindole chemistry and the dream challenge.
AU Somei, Masanori [Reprint Author]
CS Kanazawa Univ, Fac Pharmaceut Sci, Grad Sch Nat Sci and Technol, Kakuma Machi, Kanazawa, Ishikawa 9201192, Japan
syamoji_usa@dion.ne.jp
SO Yakugaku Zasshi, (APR 2008) Vol. 128, No. 4, pp. 527-563.
CODEN: YKKZAJ. ISSN: 0031-6903.
DT Article
General Review; (Literature Review)
LA Japanese
ED Entered STN: 31 Jul 2008
Last Updated on STN: 31 Jul 2008
AB We have had five dreams to challenge through our life. To meet our end,

we needed imaginary compounds, 1-hydroxytryptophans. This review describes how we had conceived the 1-hydroxyindole hypothesis, how we created a general synthetic method for 1-hydroxyindoles after 20 years' research, and how we have developed the chemistry of 1-hydroxytryptophans with full of new findings and discoveries. During the period, we defined "the efficient synthesis" and "the ideal synthesis" consisting of originality rate (OR), intellectual property factor (IPF), and application potential factor (APF). For evaluating the originality and the efficiency of the synthetic research, these indexes are more effective than both citation index and impact factor. Taking advantage of our 1-hydroxyindole chemistry, we have achieved three "ideal syntheses" approximately with high OR, IPF, and APF values. The methods employ only conventional reagents and reaction conditions without using any protecting groups. These methods made possible to produce such intellectual properties as leads for an alpha(2)-blocker, an inhibitor of platelet aggregation, an anti-osteoporosis agent, and a promising medicine for combating desertification, changing Gobi desert to the tract with full of green plants. These would be suitable for realizing our five dreams. Chemical conversion of enmein to gibberellin A(15), four-step total synthesis of optically active ergot alkaloids, and various new reactions for the synthesis of 4-substituted indoles are also involved.

L8 ANSWER 8 OF 19296 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
AN 2008:414924 BIOSIS
DN PREV200800414923
TI Predictors of DEXA use in patients with inflammatory bowel disease.
AU Etzel, Jason P.; Urson, Meaghan F.; Collins, Judith; Anawalt, Bradley D.; Dommitz, Jason A.
SO Gastroenterology, (APR 2008) Vol. 134, No. 4, Suppl. 1, pp. A500-A501.
Meeting Info.: Digestive Disease Week Meeting/109th Annual Meeting of the

American-Gastroenterological-Association. San Diego, CA, USA. May 17 -22,
2008. Amer Gastroenterol Assoc.
CODEN: GASTAB. ISSN: 0016-5085.
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LA English
ED Entered STN: 31 Jul 2008
Last Updated on STN: 31 Jul 2008
AB Aim: Inflammatory bowel disease (IBD) patients (pts) are at increased risk
for low bone mineral density (BMD). Guidelines for testing IBD pis for
low BMD with DEXA were published in 2003. Our aims were to assess
predictors of DEXA use; DEXA use pre- and post-guidelines; and to compare
DEXA results for pts with/without testing criteria. Methods: 2045 pis
with at least one IBD ICD9 code at 6 US veterans' hospitals (I tertiary
center, 5 community centers) from 1/1/94-10/27/06 were identified using
electronic records. Manual chart review was used to confirm the
diagnosis (dx) of IBD, extract DEXA results and identify fractures. Low
BMD is defined as T score < -1.0 at any site. A multivariate Cox
proportional hazards model was used to determine predictors of DEXA use,
including all variables that were significant in bivariate analysis
(p<0.1). Results: 1512 pts (74%) had confirmed IBD; only the 1215 (80%)
with greater than one yr of follow-up and no DEXA prior to IBD dx were
included. Mean age was 61.7 yrs, mean follow-up was 5.4 yrs and 94% were
male. 453 (37%) were seen at the tertiary center. 874 (72%) met criteria
for testing, but only 184 received a DEXA (21%). Results of the
multivariate model are shown in the table. Those with first IBD dx after
1/1/03 were more likely to have DEXA within 3 yrs than those with first dx
prior to 1/1/00 (29.9% vs. 8.3%, p<0.001 chi-square). Those first seen
between 2000 and 2003 had intermediate use of DEXA (23.8%). Those who met
criteria for testing had significantly greater prevalence of low BMD
compared to those who did not (77.3% vs. 56.4%, p=0.009, exact test).

Osteoporosis was common regardless of testing criteria (27% vs. 21%, p=ns). Conclusion: Although most IBD pts meet criteria for DEXA, only a minority were tested. DEXA use is increasing, possibly related to guideline release. Low BMD is very common in IBD. Further efforts at improving DEXA testing are warranted. Adjusted Hazard Ratios for Predictors of Use of DEXA (n=1215).[GRAPHICS]

L8 ANSWER 9 OF 19296 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
AN 2008:414458 BIOSIS
DN PREV200800414457
TI Is there a gender bias in surveillance for osteoporosis in IBD patients? A single center study.
AU de Silva, Punyanganie S.; Jamieson, Crawford P.
SO Gastroenterology, (APR 2008) Vol. 134, No. 4, Suppl. 1, pp. A400.
Meeting Info.: Digestive Disease Week Meeting/109th Annual Meeting of the American-Gastroenterological-Association. San Diego, CA, USA. May 17 -22, 2008. Amer Gastroenterol Assoc.
CODEN: GASTAB. ISSN: 0016-5085.
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LA English
ED Entered STN: 31 Jul 2008
Last Updated on STN: 31 Jul 2008
AB INTRODUCTION: The increased risk of IBD patients developing osteoporosis and related fractures is well established. Recently revised British Society of Gastroenterology (BSG) guidelines highlight the need for appropriate surveillance in moderate to high risk groups. While women are more likely to develop osteoporosis, men are also significantly at risk. [1] AIMS & METHODS: To assess if there is a gender bias in surveillance of patients at increased risk of developing osteoporosis. Retrospective case note review of patients with an established diagnosis of IBD >1 year's duration presenting to G1 clinics at a UK hospital over 4 weeks. Demographic data and risk factors based on current BSG guidelines were recorded and implementation of recommendations assessed. Results were compared between genders and statistical significance calculated using Chi Square analysis.
RESULTS: Total number of patients 60 (M30, F30). Age range 17-87 years.

Average age 47.2 years (M53, F43.8). Males and females were well matched.
The average disease duration was 7.32 and 7.96 years for women and men
respectively. 8 female and 5 male patients had DEXA scans (p>0.05).
Average age was 40.2(M) and 48.62yrs(F). 80% of males having DEXA scans
had disease duration of >6 yrs compared to 62.5% of females. 50% of
females and 60% of males had osteoporosis. Follow up
osteoporosis surveillance was in accordance with BSG guidelines in
60% of men and 25% of women. Physical activity was not recorded at all.
Recording of alcohol and tobacco consumption was low in both groups.
Calcium levels were checked less frequently than alkaline phosphatase in
both groups (52.3% vs 95%). 18.75% of patients checked had hypocalcaemia.
25% of men >70 yrs had Ca levels checked and 75% were on recurrent
steroids. 2 females >70yrs were on steroids. Both had calcium levels
checked, but bone density was measured only in one. None of the older men
(0/4) were considered for bisphosphonate therapy on commencement of
steroids when compared to women (1/4). 11.8%(2/17) of women and 18.2%
(2/11) of men <65 years with high risk factors were considered for
bisphosphonate therapy on commencement of steroids (p>0.05).
Documentation of lifestyle advice to minimize osteoporosis was
low. CONCLUSION: There is no significant difference between surveillance
frequency for osteoporosis amongst males and females. However,
overall surveillance remains low. Consideration of bisphosphonates,
regular monitoring of calcium levels and assessment of lifestyle factors
could be improved by an increased awareness amongst clinicians,
[1]
Jahnsen J, Falch J. Body composition in patients with inflammatory bowel
disease.

L8 ANSWER 10 OF 19296 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on
STN
AN 2008:394811 BIOSIS

DN PREV200800394810
TI Rheumatic conditions in human immunodeficiency virus infection.
AU Walker, U. A. [Reprint Author]; Tyndall, A.; Daikeler, T.
CS Univ Basel, Dept Rheumatol, Basel, Switzerland
ulrich.walker@fps-basel.ch
SO Rheumatology (Oxford), (JUL 2008) Vol. 47, No. 7, pp. 952-959.
ISSN: 1462-0324.
DT Article
General Review; (Literature Review)
LA English
ED Entered STN: 16 Jul 2008
Last Updated on STN: 16 Jul 2008
AB Many rheumatic diseases have been observed in HIV-infected persons. We,
therefore, conducted a comprehensive literature search in order to
review the prevalence, presentation and pathogenesis of rheumatic
manifestations in HIV-infected subjects. Articular conditions
(arthralgia, arthritis and SpAs) are either caused by the HIV infection
itself, triggered by adaptive changes in the immune system, or secondary
to microbial infections. Muscular symptoms may result from
rhabdomyolysis, myositis or from side-effects of highly active
anti-retroviral therapy (HAART). Osseous complications include
osteonecrosis, osteoporosis and osteomyelitis. Some conditions
such as the diffuse infiltrative lymphocytosis syndrome and sarcoidosis
affect multiple organ systems. SLE may be observed but may be difficult
to differentiate from HIV infection. Some anti-retroviral agents can
precipitate hyperuricaemia and are associated with arthralgia. When
indicated, immunosuppressants and even anti-TNF-alpha agents can be used
in the carefully monitored HIV patient. Thus, rheumatic diseases and
asymptomatic immune phenomena remain prevalent in HIV-infected persons
even after the widespread implementation of highly active anti-retroviral
therapy.

=> d his

(FILE 'HOME' ENTERED AT 15:00:59 ON 12 AUG 2008)

FILE 'BIOSIS, CAPLUS, EMBASE' ENTERED AT 15:01:13 ON 12 AUG 2008
L1 299 S HEY1 OR HEY 1
L2 83 S L1 AND (BONE OR OSTEO?)

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L3           58 DUP REM L2 (25 DUPLICATES REMOVED)

     FILE 'STNGUIDE' ENTERED AT 15:06:16 ON 12 AUG 2008

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L4         6460 S MC3T3
L5           10 S L1 AND L4
L6            6 DUP REM L5 (4 DUPLICATES REMOVED)

     FILE 'STNGUIDE' ENTERED AT 15:28:47 ON 12 AUG 2008

     FILE 'BIOSIS, CAPLUS, EMBASE' ENTERED AT 15:54:26 ON 12 AUG 2008
L7       101608 S OSTEOPOROSIS
L8        19296 S L7 AND REVIEW

=> s l7 and gene express?
   2 FILES SEARCHED...
L9         1589 L7 AND GENE EXPRESS?

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=> s l9 and review
L10         328 L9 AND REVIEW

=> d bib abs 1-10

L10  ANSWER 1 OF 328  BIOSIS  COPYRIGHT (c) 2008 The Thomson
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     STN
AN   2007:319627  BIOSIS
DN   PREV200700316582
TI   Bone metabolism and vascular calcification.
AU   Danilevicius, C. F.; Lopes, J. B.; Pereira, R. M. R. [Reprint
Author]
CS   Univ Sao Paulo, Fac Med, Disciplina Reumatol, Lab Metab Osseo,
Av Dr
     Arnaldo 455,Sala 3107,LIM-17, BR-01246903 Sao Paulo, SP, Brazil
     rosamariarp@yahoo.com
SO   Brazilian Journal of Medical and Biological Research, (APR 2007)
Vol. 40,
     No. 4, pp. 435-442.
     CODEN: BJMRDK. ISSN: 0100-879X.
DT   Article
     General Review; (Literature Review)
LA   English
ED   Entered STN: 24 May 2007
     Last Updated on STN: 24 May 2007
AB   Osteoporosis and atherosclerosis are chronic degenerative
```

diseases which have been considered to be independent and whose common characteristic is increasing incidence with age. At present, growing evidence indicates the existence of a correlation between cardiovascular disease and osteoporosis, irrespective of age. The morbidity and mortality of osteoporosis is mainly related to the occurrence of fractures. Atherosclerosis shows a high rate of morbidity and especially mortality because of its clinical repercussions such as angina pectoris, acute myocardial infarction, stroke, and peripheral vascular insufficiency. Atherosclerotic disease is characterized by the accumulation of lipid material in the arterial wall resulting from autoimmune and inflammatory mechanisms. More than 90% of these fatty plaques undergo calcification. The correlation between osteoporosis and atherosclerosis is being established by studies of the underlying physiopathological mechanisms, which seem to coincide in many biochemical pathways, and of the risk factors for vascular disease, which have also been associated with a higher incidence of low-bone mineral density. In addition, there is evidence indicating an action of antiresorptive drugs on the reduction of cardiovascular risks and the effect of statins, antihypertensives and insulin on bone mass increase. The mechanism of arterial calcification resembles the process of osteogenesis, involving various cells, proteins and cytokines that lead to tissue mineralization. The authors review the factors responsible for atherosclerotic disease that correlate with low-bone mineral density.

L10 ANSWER 2 OF 328 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
AN 2007:172087 BIOSIS
DN PREV200700161045
TI Osteoclast differentiation and gene regulation.
AU Zhao, Qingxiao; Shao, Jianzhong; Chen, Wei; Li, Yi-Ping [Reprint Author]
CS Harvard Univ, Sch Dent Med, Forsyth Inst, Dept Cytokine Biol, 140 The

Fenway, Boston, MA 02115 USA
ypli@forsyth.org
SO Frontiers in Bioscience, (JAN 1 2007) Vol. 12, pp. 2519-2529.
ISSN: 1093-9946.
DT Article
General Review; (Literature Review)
LA English
ED Entered STN: 7 Mar 2007
Last Updated on STN: 7 Mar 2007
AB Osteoclasts, the bone resorbing cells, play a key role both in normal bone remodeling and in the skeletal osteopenia of arthritis, osteoporosis, periodontal disease and certain malignancies. Osteoclast cellular commitment, differentiation and function depend upon the establishment of specific patterns of gene expression achieved through networks of transcription factors activated by osteoclastogenic cytokines. This review is an updated look at the various transcription factors and cytokines that have been demonstrated to play critical roles in osteoclast differentiation and function, along with their known animal models, such as: PU. 1, Mcsf, RANKL, NF- kappaB, AP-1, NFATc1, Mitf, Myc, and Src. Further studies on these transcription factors and cytokines will not only expand our basic understanding of the molecular mechanisms of osteoclast differentiation, but will also aid our ability to develop therapeutic means of intervention in osteoclast-related diseases.

L10 ANSWER 3 OF 328 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
AN 2007:52185 BIOSIS
DN PREV200700052760
TI Advances in Runx2 regulation and its isoforms.
AU Li, Ya-lin; Xiao, Zhou-sheng [Reprint Author]
CS Univ Kansas, Med Ctr, Kidney Inst, 6108 WHE,3901 Blvd, Kansas City, KS 66160 USA
xiaozs64@hotmail.com
SO Medical Hypotheses, (2007) Vol. 68, No. 1, pp. 169-175.
CODEN: MEHYDY. ISSN: 0306-9877.
DT Article
General Review; (Literature Review)
LA English
ED Entered STN: 10 Jan 2007
Last Updated on STN: 10 Jan 2007

AB During the last 10 years, we have witnessed major progress in skeleton biology. Runx2 is an accepted transcription factor essential for osteoblast development from mesenchymal stem cells and maturation into osteocytes and organize crucial events during bone formation. Alternations in Runx2 expression levels are associated with skeletal diseases. In vitro and in vivo studies have reported that multiple integrated complex path ways (such as Wnt/LRP5/beta-catenin, BMP/Smads, 1, 25-(OH)2-vitaminD3/VDR/VDRE pathway, etc.) and several regulatory proteins (such as Msx2, Dlx5, Twists, etc.) play critical roles in modulating Runx2 gene expression, activity, and the subsequent bone formation. These findings provide novel insights through controlling osteoblast differentiation to treat osteoporosis or other bone diseases with altered bone mass by stimulating Runx2 expression. Further studies have shown that expression of RUNX2 is initiated from two promoters, the distal P1 promoter and the proximal P2 promoter. The alternative use of promoters gives rise to the genesis of two major protein isoforms with distinct amino termini, named as Runx2-Typel and Runx2-Typell. Here, we also review a complex spatio-temporal pattern of two major isoforms expressions and their possible function differences in skeleton development.

L10 ANSWER 4 OF 328 BIOSIS
AN 2006:593690 BIOSIS
DN PREV200600590153
TI Nuclear receptors: Potential biomarkers for assessing physiological functions of soy proteins and phytoestrogens.
AU Xiao, Chao Wu [Reprint Author]; Wood, Carla; Gilani, C. Sarwar
CS Hlth Canada, Hlth Prod and Food Branch, Nutr Res Div, Food Directorate, Ottawa, ON K1A 0L2, Canada
chaowu_xiao@hc-sc.gc.ca
SO Journal of AOAC International, (JUL-AUG 2006) Vol. 89, No. 4, pp. 1207-1214.
ISSN: 1060-3271.

DT Article
LA English
ED Entered STN: 8 Nov 2006
Last Updated on STN: 8 Nov 2006
AB Soy consumption is associated with decreased incidence of chronic diseases, including cardiovascular diseases, atherosclerosis, diabetes, osteoporosis, and certain types of cancers. However, consumption of high amounts of soy isoflavones may adversely influence endocrine functions, such as thyroid function and reproductive performance, because of their structural similarity to endogenous estrogens. Nuclear receptors are a group of transcription factors that play critical roles in the regulation of gene expression and physiological functions through direct interaction with target genes. Modulation of the abundance of these receptors, such as changing their gene expression, alters the sensitivity of the target cells or tissues to the stimulation of ligands, and eventually affects the relevant physiological functions, such as growth, development, osteogenesis, immune response, lipogenesis, reproductive process, and anticarcinogenesis. A number of studies have shown that the bioactive components in soy can modify the expression of these receptors in various tissues and cancer cells, which is believed to be a key intracellular mechanism by which soy, components affect physiological functions' This review summarizes the current understanding of the modulation of nuclear receptors by soy proteins and isoflavones, and focuses especially on the receptors for estrogens, progesterone, androgen, vitamin D, retinoic acid, and thyroid hormones as well as the potential impact on physiological functions.

L10 ANSWER 5 OF 328 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
AN 2006:432632 BIOSIS
DN PREV200600425425
TI The molecular inflammatory process in aging.
AU Chung, Hae Young [Reprint Author]; Sung, Bokyung; Jung, Kyung Jin; Zou, Yani; Yu, Byung Pal

CS Pusan Natl Univ, Coll Pharm, Pusan 609735, South Korea
hyjung@pusan.ac.kr
SO ANTIOXIDANTS & REDOX SIGNALING, (MAR-APR 2006) Vol. 8, No. 3-4, pp.
572-581.
ISSN: 1523-0864.
DT Article
General Review; (Literature Review)
LA English
ED Entered STN: 30 Aug 2006
Last Updated on STN: 30 Aug 2006
AB Emerging pathological evidence indicates that major chronic aging-related
diseases such as atherosclerosis, arthritis, dementia, osteoporosis, and cardiovascular diseases, are in flammation-related. In this review, inflammation is examined as a possible underlying basis for the molecular alterations that link aging
and age-related pathological processes. A proposal for the molecular
inflammation hypothesis of the aging views the redox derangement that
occurs during aging as the major factor for increased risk for age-related
inflammation. Accumulated data strongly indicate the activation of
redox-sensitive transcription factors and dysregulated gene expression under the age-related oxidative stress seems to be the major culprits. Key players involved in the inflammatory process are the
age-related upregulation of NF-kappa B, IL-1 beta, IL-6, TNF alpha,
cyclooxygenase-2, adhesion molecules, and inducible NO synthase. Furthermore, data are presented on the molecular events involved in
age-related NF-kappa B activation and phosphorylation by I kappa B
kinase/NIK and MAPKs. Experimental data on antiaging calorie restriction
(CR) for its antiinflammatory efficacy by suppressing the upregulated
proinflammatory mediators will be reviewed. Also, the involvement of
another super family of transcription factors, PPARs (PPAR alpha, gamma)
as regulators of proinflammatory responses and NF-kappa B signaling
pathway is described as well as a discussion on the physiological
significance of a well-maintained balance between NF-kappa B and PPARs.

L10 ANSWER 6 OF 328 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on

STN
AN 2006:407795 BIOSIS
DN PREV200600402387
TI Bone tissue engineering by gene delivery.
AU Kofron, Michelle D.; Laurencin, Cato T. [Reprint Author]
CS 400 Ray C Hunt Dr,Suite 330, Charlottesville, VA 22903 USA
CTL3F@virginia.edu
SO Advanced Drug Delivery Reviews, (JUL 7 2006) Vol. 58, No. 4, pp. 555-576.
CODEN: ADDREP. ISSN: 0169-409X.
DT Article
LA English
ED Entered STN: 17 Aug 2006
Last Updated on STN: 17 Aug 2006
AB Recombinant human bone morphogenetic protein-2 and -7 were recently granted United States Food and Drug Administration approval for select clinical applications in bone repair. While significant progress has been made in the delivery of recombinant osteogenic factor to promote bone healing, the short half-life and instability of the protein requires the delivery of milligram quantities of factor or multiple dosages. The potential of gene therapy for bone regeneration is the delivery of physiological levels of therapeutic protein using natural cellular mechanisms. Experimental investigations have demonstrated this approach uses lower dosages of factor to yield bone healing equivalent to that achieved via the administration of recombinant factor or use of bone grafts. The current states of gene delivery for bone tissue engineering applications and challenges to be met are presented in this review .Over the past couple of years, studies have continued to examine the delivery of the osteogenic factor bone morphogenetic protein using gene therapies. The importance of angiogenesis to bone formation has prompted the development of vascular endothelial growth factor gene expression systems for bone regeneration. Viral vectors, in combination with allograft bone, have been investigated to improve existing surgical care. Newly constructed vectors with reduced immunogenicity and regulated gene expression systems

provide a greater degree of control over the timing and level of gene expression. Several advances have allowed bone tissue engineering by gene delivery to advance beyond serving as a potential treatment for isolated bone defects and fractures to a gene therapy approach for the treatment of genetic based bone diseases, such as osteogenesis imperfecta. (c) 2006 Elsevier B.V. All rights reserved.

L10 ANSWER 7 OF 328 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
AN 2006:400145 BIOSIS
DN PREV200600400588
TI Inflammation and immune regulation by 12/15-lipoxygenases.
AU Kuehn, Hartmut; O'Donnell, Valerie B. [Reprint Author]
CS Cardiff Univ, Dept Med Biochem and Immunol, Heath Pk, Cardiff CF14 4XN, UK
o-donnellvb@cardiff.ac.uk
SO Progress in Lipid Research, (JUL 2006) Vol. 45, No. 4, pp. 334-356.
CODEN: PLIRDW. ISSN: 0163-7827.
DT Article
LA English
ED Entered STN: 9 Aug 2006
Last Updated on STN: 9 Aug 2006
AB 12/15-Lipoxygenases (12/15-LOX) are members of the LOX family, which are expressed in mammals by monocytes and macrophages following induction by the T helper type 2 cytokines, interleukins-4 and -13. They oxygenate free polyenoic fatty acids but also ester lipids and even complex lipid-protein assemblies such as biomembranes and lipoproteins. The primary oxidation products are either reduced by glutathione peroxidases to corresponding hydroxy derivatives or metabolized into secondary oxidized lipids including leukotrienes, lipoxins and hepoxilins, which act as lipid mediators. Examination of knockout and transgenic animals revealed important roles for 12/15-LOX in inflammatory diseases, including atherosclerosis, cancer, osteoporosis, angiotension II-dependent hypertension and diabetes. In vitro studies suggested 12/15-LOX products as coactivators of peroxisomal proliferator activating-receptors (PPAR),

regulators of cytokine generation, and modulators of gene expression related to inflammation resolution. Despite much work in this area, the biochemical mechanisms by which 12/15-LOX regulates physiological and pathological immune cell function are not fully understood. This review will summarize the biochemistry and tissue expression of 12/15-LOX and will describe the current knowledge regarding its immunobiology and regulation of inflammation. (c) 2006 Elsevier Ltd. All rights reserved.

L10 ANSWER 8 OF 328 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
AN 2006:184902 BIOSIS
DN PREV200600191427
TI World Review of Nutrition and Dietetics.
AU Simopoulos, AP [Editor]
SO Simopoulos, AP [Editor]. World Rev. Nutr. Diet., (2005) World Review of Nutrition and Dietetics. Publisher: KARGER, POSTFACH, CH-4009 BASEL, SWITZERLAND. Series: WORLD REVIEW OF NUTRITION AND DIETETICS. CODEN: WRNDAT. ISSN: 0084-2230. ISBN: 3-8055-7945-4(H).
DT Book
LA English
ED Entered STN: 15 Mar 2006
Last Updated on STN: 15 Mar 2006
AB This 182-page book is based on the proceedings of the Fifth International Conference on Nutrition and Fitness, entitled 'Nutrition and Fitness: Mental Health, Aging, and the Implementation of a Healthy Diet and Physical Activity Lifestyle', which was held in Athens in June 2004. This book is volume 95 in the series World Review in Nutrition and Dietetics and is volume 2 of the subseries Nutrition and Fitness. Despite the enormous interest in discovering longevity genes in humans, the results have been elusive, while the effects of physical activity in delaying aging are promising and the importance of caloric restriction is now being systematically investigated. Currently there is enough evidence to define components of a healthy diet and physical activity lifestyle at the population level and it is clear that lack of exercise is associated

with increased risk of premature chronic disease and death. Research now aims at defining the type and frequency of genetic variation and its influence on dietary response as well as the impact of diet and exercise on gene expression. This book is structured into 5 sections based on the proceedings of the conference and contains 17 individually-authored reviews or papers. The text is in English. The first section contains a keynote address on exploring the relevant parameters of positive health. The second section of the book focuses on mental health and there are 2 papers in this section that individually discuss psychiatric disorders, mood and cognitive function in terms of the influences of nutrients and physical activity, and nutrition and schizophrenia. Aging, osteoporosis and physical activity is the theme of the third section and individual papers in this section discuss: the role of physical activity in managing obesity after menopause; osteoporosis as a complex disorder of aging with multiple genetic and environmental determinants; changes in dietary fatty acids and lifestyle as major factors for rapidly increasing inflammatory diseases and elderly-onset diseases; an overview of physical activity for health; and physical inactivity as a disease. Defining the components of a healthy diet and physical activity for health is the focus of the fourth section and the 5 papers in this section individually discuss the diet in Greece, the health importance of a balance of omega-6/omega-3 essential fatty acids, dietary prevention of coronary heart disease and the Lyon Diet Heart Study, the Nicotera diet as the reference Italian Mediterranean diet, and the evidence and mechanisms of the health benefits associated with moderate wine consumption. The fifth section focuses on the role of government in implementing a healthy diet and physical activity lifestyle and there are 4 papers in this final section. These 4 papers individually

discuss: the implications of food regulations for novel foods; intersectoral partnerships supporting a healthy diet and active lifestyle, and the Centre of Excellence in Functional Foods in Australia, which combines industry, science and practice; why there is a need for a global strategy on diet, physical activity and health; and finally nutrition and fitness policies in the United States. The book is indexed by author and by subject and contains 19 figures, 1 of which is in color, and 26 tables. This book will be of interest to researchers, physicians, exercise physiologists, geneticists, dietitians, food scientists, policy makers in government, private industry and international organizations, and public health workers worldwide.

L10 ANSWER 9 OF 328 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
AN 2005:543158 BIOSIS
DN PREV200510329923
TI Proceedings from the "Third International Conference on Mechanism of Action of Nutraceuticals".
AU Mandel, Silvia; Packer, Lester; Youdim, Moussa B. H.; Weinreb, Orly [Reprint Author]
CS Technion Israel Inst Technol, Fac Med, Dept Pharmacol, Rappaport Family Res Inst, POB 9697, IL-31096 Haifa, Israel packer@usc.edu; worly@tx.technion.ac.il
SO Journal of Nutritional Biochemistry, (SEP 2005) Vol. 16, No. 9, pp. 513-520. CODEN: JNBIEL. ISSN: 0955-2863.
DT Article General Review; (Literature Review)
LA English
ED Entered STN: 1 Dec 2005 Last Updated on STN: 1 Dec 2005
AB The "Third International Conference on Mechanisms of Action of Nutraceuticals" (ICMAN 3) was held to bring investigators from around the world together to find answers and share experience relevant to the role of nutraceuticals in health and disease. Dietary supplements are currently receiving recognition as being beneficial in coronary heart

disease, cancer, osteoporosis and other chronic and degenerative diseases such as diabetes, Parkinson's and Alzheimer's diseases. This gave impetus to investigate the mechanisms of action of nutraceuticals and related bioactive compounds in disease pathologies. Many lines of evidence indicate that the mechanistic actions of natural compounds involve a wide array of biological processes, including activation of antioxidant defenses, signal transduction pathways, cell survival-associated gene expression, cell proliferation and differentiation and preservation of mitochondrial integrity. Furthermore, many of these compounds exert anti-inflammatory actions through inhibition of oxidative stress-induced transcription factors (e.g., NF-kappa B, AP-1), cytotoxic cytokines and cyclooxygenase-2. It appears that these properties play a crucial role in the protection against the pathologies of numerous age-related or chronic diseases. This review summarizes the latest research finding in functional foods and micronutrients in the promotion of health and reduction of risk for major chronic diseases as presented in this symposium.

L10 ANSWER 10 OF 328 BIOSIS
AN 2005:194469 BIOSIS
DN PREV200500197617
TI Role of regucalcin in maintaining cell homeostasis and function (Review).
AU Yamaguchi, Masayoshi [Reprint Author]
CS Grad Sch Nutr SciLab Endocrinol and Mol Metab, Univ Shizouka, 52-1 Yada, Shizouka, 4228526, Japan
yamaguch@u-shizuoka-ken.ac.jp
SO International Journal of Molecular Medicine, (March 2005) Vol. 15, No. 3, pp. 371-389. print.
ISSN: 1107-3756 (ISSN print).
DT Article
LA English
ED Entered STN: 25 May 2005
Last Updated on STN: 25 May 2005
AB Regucalcin was discovered in 1978 as a Ca2+- binding protein that does not

contain EF-hand motif of Ca2+-binding domain. The name regucalcin was proposed for this Ca2+-binding protein, which can regulate liver cell functions related to Ca2+. The regucalcin gene is localized on chromosome X. and the organization of the regucalcin gene consists of seven exons and six introns. AP-1 and NFI-A1 can bind to the promoter region of the rat regucalcin gene to mediate the Ca2+ response for transcriptional activation. Regucalcin plays a pivotal role in maintaining intracellular Ca2+ homeostasis due to activating Ca2+ pump enzymes in the plasma membrane (basolateral membrane), microsomes (endoplasmic reticulum) and mitochondria of many cell types. Regucalcin has a suppressive effect on Ca2+ signaling from the cytoplasm to the nucleus in the proliferative cells. Also, regucalcin has been demonstrated to transport to nucleus, and it can inhibit nuclear protein kinase, protein phosphatase, and deoxyribonucleic acid (DNA) and ribonucleic acid (RNA) synthesis. Regucalcin can control enhancement of cell proliferation due to hormonal stimulation. Moreover, overexpression of regucalcin suppresses cell death and apoptosis in the cloned rat hepatoma cells induced by various signaling factors. Regucalcin plays a multifunctional role in the regulation of cellular function in liver, kidney cortex, heart and brain. Moreover, regucalcin-overexpressing rat has been shown to induce bone loss and hyperlipidemia with increasing age, indicating a pathophysiologic role. Regucalcin transgenic rat may be useful as an animal model in osteoporosis and hyperlipidemia. Thus, regucalcin plays a pivotal role in maintaining cell homeostasis and function. Regucalcin gene expression-related diseases may be found in human.

=> FIL STNGUIDE

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=> FIL BIOSIS CAPLUS EMBASE
COST IN U.S. DOLLARS                              SINCE FILE      TOTAL
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CA SUBSCRIBER PRICE                                   0.00
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     (FILE 'HOME' ENTERED AT 15:00:59 ON 12 AUG 2008)

     FILE 'BIOSIS, CAPLUS, EMBASE' ENTERED AT 15:01:13 ON 12 AUG 2008
L1           299 S HEY1 OR HEY 1
L2            83 S L1 AND (BONE OR OSTEO?)
L3            58 DUP REM L2 (25 DUPLICATES REMOVED)

     FILE 'STNGUIDE' ENTERED AT 15:06:16 ON 12 AUG 2008

     FILE 'BIOSIS, CAPLUS, EMBASE' ENTERED AT 15:26:59 ON 12 AUG 2008
L4          6460 S MC3T3
L5            10 S L1 AND L4
L6             6 DUP REM L5 (4 DUPLICATES REMOVED)

     FILE 'STNGUIDE' ENTERED AT 15:28:47 ON 12 AUG 2008

     FILE 'BIOSIS, CAPLUS, EMBASE' ENTERED AT 15:54:26 ON 12 AUG 2008
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L7       101608 S OSTEOPOROSIS
L8        19296 S L7 AND REVIEW
L9         1589 S L7 AND GENE EXPRESS?
L10         328 S L9 AND REVIEW

     FILE 'STNGUIDE' ENTERED AT 16:13:27 ON 12 AUG 2008

     FILE 'BIOSIS, CAPLUS, EMBASE' ENTERED AT 16:15:39 ON 12 AUG 2008

=> s l10 and (hey1 or hey 1)
L11           0 L10 AND (HEY1 OR HEY 1)

=> s l7 (hey1 or hey 1)
MISSING OPERATOR 'L22 (HEY1'
The search profile that was entered contains terms or
nested terms that are not separated by a logical operator.

=> s l7 and (hey1 or hey 1)
L12           4 L7 AND (HEY1 OR HEY 1)

=> dup rem l12
PROCESSING COMPLETED FOR L12
L13           3 DUP REM L12 (1 DUPLICATE REMOVED)

=> d bib abs 1-
YOU HAVE REQUESTED DATA FROM 3 ANSWERS - CONTINUE? Y/(N):y

L13  ANSWER 1 OF 3  BIOSIS  COPYRIGHT (c) 2008 The Thomson
Corporation  on STN
AN   2006:92025  BIOSIS
DN   PREV200600089626
TI   Detection of homocysteine and cysteine.
AU   Wang, Weihua; Rusin, Oleksandr [Reprint Author]; Xu, Xiangyang;
Kim,
     Kwang; Escobedo, Jorge O.; Fakayode, Sayo O.; Fletcher, Kristin
A.; Lowry,
     Mark; Schowalter, Corin M.; Lawrence, Candace M.; Fronczek,
Frank R.;
     Warner, Isiah M.; Strongin, Robert M.
CS   Louisiana State Univ, Dept Chem, Baton Rouge, LA 70803 USA
     rstrong@lsu.edu
SO   Journal of the American Chemical Society, (NOV 16 2005) Vol.
127, No. 45,
     pp. 15949-15958.
     CODEN: JACSAT. ISSN: 0002-7863.
DT   Article
LA   English
ED   Entered STN: 25 Jan 2006
     Last Updated on STN: 25 Jan 2006
AB   At elevated levels, homocysteine (Hey, 1) is a risk
     factor for cardiovascular diseases, Alzheimer's disease, neural
tube
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defects, and osteoporosis. Both 1 and cysteine (Cys, 3) are linked to neurotoxicity. The biochemical mechanisms by which 1 and 3 are involved in disease states are relatively unclear. Herein, we describe simple methods for detecting either Hey or Cys in the visible spectral region with the highest selectivity reported to date without using biochemical techniques or preparative separations. Simple methods and readily available reagents allow for the detection of Cys and Hey in the range of their physiologically relevant levels. New HPLC postcolumn detection methods for biological thiols are reported. The potential biomedical relevance of the chemical mechanisms involved in the detection of 1 is described.

L13 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2004:878503 CAPLUS
DN 141:344623
TI Gene expression profile associated with osteoblast differentiation and osteoporosis diagnosis markers
IN Susa Spring, Mira; Zamurovic, Natasa
PA Novartis A.-G., Switz.; Novartis Pharma G.m.b.H.
SO PCT Int. Appl., 75 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004090161	A1	20041021	WO 2004-EP3588	20040405

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TD, TG
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EP 1923401 A2 20080521 EP 2007-119293 20040405
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US 20070105101 A1 20070510 US 2005-552319 20051018
US 20080118521 A1 20080522 US 2007-924367 20071025
PRAI US 2003-462834P P 20030414
EP 2004-725691 A3 20040405
WO 2004-EP3588 W 20040405
US 2005-552319 A1 20051018

AB He present invention relates to the elucidation of the global changes in gene expression during osteoblastic differentiation of MC3T3-E1 cell line, in particular MC3T3-1b clone. In one aspect, the present invention relates to detecting a change in an expression level of one or more genes or gene families associated with the differentiation of MC3T3-E1 cells, in particular MC3T3-1 b cells, into osteoblasts. The genes identified may be used as markers for osteoporosis diagnosis or monitoring the treatment of a patient with osteoporosis.

RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2008 ACS on STN DUPLICATE 1
AN 2004:511739 CAPLUS
DN 141:120681
TI Identification of novel regulators associated with early-phase osteoblast

differentiation
AU de Jong, Diana S.; Vaes, Bart L. T.; Dechering, Koen J.; Feijen, Alie;
Hendriks, Jose M. A.; Wehrens, Ron; Mummery, Christine L.; van Zoelen,
Everardus J. J.; Olijve, Wiebe; Steegenga, Wilma T.
CS Department of Applied Biology, University of Nijmegen, Nijmegen, Neth.
SO Journal of Bone and Mineral Research (2004), 19(6), 947-958
CODEN: JBMREJ; ISSN: 0884-0431
PB American Society for Bone and Mineral Research
DT Journal
LA English
AB Key regulatory components of the BMP-induced osteoblast differentiation
cascade remain to be established. Microarray and subsequent expression
analyses in mice identified two transcription factores, Hey1 and
Tcf7, with in vitro and in vivo expression characteristics very similar to
Cbfa1. Transfection studies suggest that Tcf7 modulates BMP2-induces
osteoblast differentiation. This study contributes to a better definition
of the onset of BMP-induced osteoblast differentiation. Introduction:
Elucidation of the genetic cascade guiding mesenchymal stem cells to
become osteoblasts is of extreme importance for improving the treatment of
bone-related diseases such as osteoporosis. The aim of this
study was to identify regulators of the early phases of bone morphogenetic
protein (BMP)2-induced osteoblast differentiation. Materials and Methods:
Osteoblast differentiation of mouse C2C12 cells was induced by treatment
with BMP2, and regulation of gene expression was studied during the
subsequent 24 h using high-d. microarrays. The regulated genes were
grouped by means of model-based clustering, and protein functions were
assigned. Real-time quant. RT-PCR anal. was used to validate BMP2-induced
gene expression patterns in C2C12 cells. Osteoblast specificity was
studied by comparing these expression patterns with those in C3H10T1/2 and
NIH3T3 cells under similar conditions. In situ hybridization of mRNA in
embryos at embryonic day (E)14.5 and E16.5 of gestation and on newborn

mouse tails were used to study in vivo expression patterns. Cells
constitutively expressing the regulated gene Tcf7 were used to investigate
its influence on BMP-induced osteoblast differentiation. Results and
Conclusions: A total of 184 genes and expressed sequence tags (ESTs) were
differentially expressed in the first 24 h after BMP2 treatment and
grouped in subsets of immediate early, intermediate early, and late early
response genes. Signal transduction regulatory factors mainly represented
the subset of immediate early genes. Regulation of expression of these
genes was direct, independent of de novo protein synthesis and independent
of the cell type studied. The intermediate early and late early genes
consisted primarily of genes related to processes that modulate morphol.,
basement membrane formation, and synthesis of extracellular calcified
matrix. The late early genes require de novo protein synthesis and show
osteoblast specificity. In vivo and in vitro expts. showed that the
transcription factors Hey1 and Tcf7 exhibited expression
characteristics and cell type specificity very similar to those of the
osteoblast specific transcription factor Cbfa1, and constitutive
expression of Tcf7 in C2C12 cells differentially regulated osteoblast
differentiation marker genes.
RE.CNT 58 THERE ARE 58 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> FIL STNGUIDE

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
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CA SUBSCRIBER PRICE	0.00	

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                   sequence search option
 NEWS 13  JUN 06   EPFULL enhanced with 260,000 English abstracts
 NEWS 14  JUN 06   KOREAPAT updated with 41,000 documents
 NEWS 15  JUN 13   USPATFULL and USPAT2 updated with 11-character
                   patent numbers for U.S. applications
 NEWS 16  JUN 19   CAS REGISTRY includes selected substances from
                   web-based collections
 NEWS 17  JUN 25   CA/CAplus and USPAT databases updated with IPC
                   reclassification data
 NEWS 18  JUN 30   AEROSPACE enhanced with more than 1 million U.S.
                   patent records
 NEWS 19  JUN 30   EMBASE, EMBAL, and LEMBASE updated with additional
                   options to display authors and affiliated
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 NEWS 20  JUN 30   STN on the Web enhanced with new STN AnaVist
                   Assistant and BLAST plug-in
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EPFULL
 NEWS 22  JUL 28   CA/CAplus patent coverage enhanced
 NEWS 23  JUL 28   EPFULL enhanced with additional legal status
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                  information from the epoline Register
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enhancements
 NEWS 25  JUL 28  STN Viewer performance improved
 NEWS 26  AUG 01  INPADOCDB and INPAFAMDB coverage enhanced

 NEWS EXPRESS JUNE 27 08 CURRENT WINDOWS VERSION IS V8.3,
              AND CURRENT DISCOVER FILE IS DATED 23 JUNE 2008.

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=> s hesr1 or htr1 or herp2 or hesr 1
L1          174 HESR1 OR HTR1 OR HERP2 OR HESR 1

=> s l1 and (bone or osteo?)
L2           25 L1 AND (BONE OR OSTEO?)

=> dup rem l2
PROCESSING COMPLETED FOR L2
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L3            13 DUP REM L2 (12 DUPLICATES REMOVED)

=> d bib abs 1-
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L3   ANSWER 1 OF 13  CAPLUS  COPYRIGHT 2008 ACS on STN
AN   2008:289847  CAPLUS
DN   148:299881
TI   Cancer treatment with gamma-secretase inhibitors
IN   Eberhart, Charles; Fan, Xing; Maitra, Anirban
PA   The Johns Hopkins University, USA
SO   U.S. Pat. Appl. Publ., 64pp.
     CODEN: USXXCO
DT   Patent
LA   English
FAN.CNT 1
     PATENT NO.          KIND   DATE        APPLICATION NO.
DATE
     ---------------     ----   --------    --------------------
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PI   US 20080058316       A1    20080306    US 2007-712292
20070227
     WO 2007100895        A3    20080717    WO 2007-US5362
20070227
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GB, GD,
             GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG,
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             KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD,
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             RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN,
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LU, LV,
             MC, NL, PL, PT, RO, SE, SI, SK, TR, OA, BF, BJ, CF, CG,
CI, CM,
             GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
PRAI US 2006-777110P      P     20060227
     US 2006-786312P      P     20060327
OS   MARPAT 148:299881
GI
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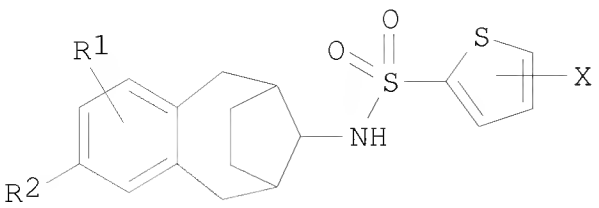

I

AB Provided are methods for treating cancer in a patient, comprising administering to a patient in need thereof a therapeutically effective regimen, the regimen comprising administering a gamma-secretase inhibitor, wherein the regimen results in a reduction in the cancer cell population in the patient. In some embodiments of the methods, the therapeutically effective regimen stabilizes, reduces or eliminates the cancer stem cell population. Also provided are compds. of the formula (I) or a pharmaceutically acceptable salt thereof, wherein R1 = H, halogen, OH, etc.; R2 = radical, etc.; and X = halo. Administration of β-secretase inhibitor GSI-18 blocked the Notch signaling pathway and reduced glioblastoma growth by targeting cancer stem cells. Overexpression of Notch2 increased tumor growth in vitro supporting strategies which target this protein for treatment of cancer.

L3 ANSWER 2 OF 13 CAPLUS COPYRIGHT 2008 ACS on STN DUPLICATE 1
AN 2007:348876 CAPLUS
DN 147:49074
TI Hesr1 and Hesr2 regulate atrioventricular boundary formation in the developing heart through the repression of Tbx2
AU Kokubo, Hiroki; Tomita-Miyagawa, Sachiko; Hamada, Yoshio; Saga, Yumiko
CS Division of Mammalian Development, National Institute of Genetics, 1111 Yata, Mishima Shizuoka, 411-8540, Japan
SO Development (Cambridge, United Kingdom) (2007), 134(4), 747-755 CODEN: DEVPED; ISSN: 0950-1991
PB Company of Biologists Ltd.
DT Journal
LA English
AB The establishment of chamber specificity is an essential requirement for cardiac morphogenesis and function. Hesr1 (Hey1) and Hesr2 (Hey2) are specifically expressed in the atrium and ventricle, resp., implicating these genes in chamber specification. In our current study,

we show that the forced expression of Hesr1 or Hesr2 in the entire cardiac lineage of the mouse results in the reduction or loss of the atrioventricular (AV) canal. In the Hesr1-misexpressing heart, the boundaries of the AV canal are poorly defined, and the expression levels of specific markers of the AV myocardium, Bmp2 and Tbx2, are either very weak or undetectable. More potent effects were observed in Hesr2-misexpressing embryos, in which the AV canal appears to be absent entirely. These data suggest that Hesr1 and Hesr2 may prevent cells from expressing the AV canal-specific genes that lead to the precise formation of the AV boundary. Our findings suggest that Tbx2 expression might be directly suppressed by Hesr1 and Hesr2. Furthermore, we find that the expression of Hesr1 and Hesr2 is independent of Notch2 signaling. Taken together, our data demonstrate that Hesr1 and Hesr2 play crucial roles in AV boundary formation through the suppression of Tbx2.

RE.CNT 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 3 OF 13 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
DUPLICATE 2
AN 2007:203797 BIOSIS
DN PREV200700196794
TI CCN3/NOV inhibits BMP-2-induced osteoblast differentiation by interacting with BMP and Notch signaling pathways.
AU Minamizato, Tokutaro; Sakamoto, Kei; Liu, Tingjiao; Kokubo, Hiroki; Katsube, Ken-ichi; Perbal, Bernard; Nakamura, Seiji; Yamaguchi, Akira
[Reprint Author]
CS Tokyo Med and Dent Univ, Grad Sch, Sect Oral Pathol, Bunkyo Ku, 1-5-45 Yushima, Tokyo 1138549, Japan
akira.mpa@tmd.ac.jp
SO Biochemical and Biophysical Research Communications, (MAR 9 2007) Vol. 354, No. 2, pp. 567-573.
CODEN: BBRCA9. ISSN: 0006-291X.
DT Article
LA English
ED Entered STN: 21 Mar 2007
Last Updated on STN: 21 Mar 2007
AB We elucidate the role of CCN3/NOV, a member of the CCN family proteins, in osteoblast differentiation using MC3T3-E1 osteoblastic

cells. Transduction with CCN3 adenovirus (AdCCN3) alone induced no apparent changes in the expression of osteoblast-related markers, whereas cotransduction with BMP-2 adenovirus (AdBMP-2) and AdCCN3 significantly inhibited the AdBMP-2-induced mRNA expression of Runx2, osterix, ALP, and osteocalcin. Immunoprecipitation-western analysis revealed that CCN3 associated with BMP-2. Compared to transduction with AdBMP-2 alone, cotransduction with AdBMP-2 and AdCCN3 attenuated the expression of phosphorylated Smad1/5/8 and the mRNA for Id1, M2, and M3. Transduction with AdCCN3 stimulated the expression of cleaved Notch1, the mRNA expression of Hes1 and Hey1/Hesr1, and the promoter activities of Hes1 and Hey1. The inhibitory effects of CCN3 on the expression of BMP-2-induced osteoblast-related markers were nullified in Hey1-deficient osteoblastic cells. These results indicate that CCN3 exerts inhibitory effects on BMP-2-induced osteoblast differentiation by its involvement of the BMP and Notch signaling pathways.

L3 ANSWER 4 OF 13 BIOSIS
AN 2008:330043 BIOSIS
DN PREV200800330042
TI GATA and BCLx1 Downregulation in erythropoiesis during in vitro lineage specific differentiation of MDS hematopoietic progenitor cells is not induced by activated notch pathway.
AU Hopfer, Olaf J. [Reprint Author]; Komor, Martina; Koehler, Ina S. N.; Freitag, Claudia; Hoelzer, Dieter; Thiel, Eckhard; Hofmann, Wolf-Karsten
CS Charite Univ Med Berlin, Dept Hematol and Oncol, Berlin, Germany
SO Blood, (NOV 16 2007) Vol. 110, No. 11, Part 2, pp. 98B-99B. Meeting Info.: 49th Annual Meeting of the American-Society-of-Hematology. Atlanta, GA, USA. December 08 -11, 2007. Amer Soc Hematol. CODEN: BLOOAW. ISSN: 0006-4971.
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LA English
ED Entered STN: 5 Jun 2008
Last Updated on STN: 5 Jun 2008
AB Notch signals have recently been shown to inhibit erythroid and megakaryocytic differentiation of hematopoietic progenitor cells. In

myelodysplastic syndrome (MDS) its role in dyserythropoiesis has not been fully elucidated. Therefore we asked whether dysregulation of Notch pathway elements might be associated with impaired GATA1 and BCLx1 expression and ineffective erythropoiesis being a hallmark of MDS hematopoiesis. We have generated an in-vitro model of MDS lineage-specific hematopoietic differentiation by culturing CD34+ bone marrow cells from healthy donors (n=7) and MDS patients (low risk: RA/n=6, RARS/n=3; high risk: RAEB/n=4, RAEB-T/n=2) with EPO and TPO. Cell harvest was at days 0, 4, 7 and 11. Expression of GATA 1, BCLx1, DLK1, Notch1, HES1 and HERP2 was measured by real time RT-PCR (qPCR). RNA expression of GATA I and of BCLx1 was steadily upregulated, particularly during late normal erythropoiesis. During normal megakaryopoiesis expression of both genes was up to 50 times lower as compared to normal erythropoiesis. In contrast, during MDS erythropoiesis a loss of typical late upregulation of GATA1 and BCLx1 was observed. DLK1 expression during erythropoiesis showed increased expression particularly in high risk MDS vs. normal controls. Expression of HES1 was increasing during the course of normal erythropoietic and megakaryopoietic differentiation but not in lineage specific cells from MDS patients. In conclusion our data show that the central erythropoietic transcription factor GATA1 and the associated antiapoptotic molecule BCLx1 are markedly downregulated during MDS erythropoiesis which may contribute to the ineffective erythropoiesis seen in this disease. Increased DLK1 expression in differentiated stem cells from high risk MDS patients was seen. However, an upregulation of the Notch pathway leading to increased expression of the GATA1 repressor HES1 could not be detected.

L3 ANSWER 5 OF 13 CAPLUS COPYRIGHT 2008 ACS on STN DUPLICATE 3
AN 2006:547542 CAPLUS
DN 145:60627
TI Activation of notch1 signaling in cardiogenic mesoderm induces abnormal heart morphogenesis in mouse
AU Watanabe, Yusuke; Kokubo, Hiroki; Miyagawa-Tomita, Sachiko; Endo, Maho;

Igarashi, Katsuhide; Aisaki, Kenichi; Kanno, Jun; Saga, Yumiko
CS Division of Mammalian Development, National Institute of Genetics, Yata
1111, Mishima, 411-8540, Japan
SO Development (Cambridge, United Kingdom) (2006), 133(9), 1625-1634
CODEN: DEVPED; ISSN: 0950-1991
PB Company of Biologists Ltd.
DT Journal
LA English
AB Notch signaling is implicated in many developmental processes. In our current study, we have employed a transgenic strategy to investigate the role of Notch signaling during cardiac development in the mouse. Cre recombinase-mediated Notch1 (NICD1) activation in the mesodermal cell lineage leads to abnormal heart morphogenesis, which is characterized by deformities of the ventricles and atrioventricular (AV) canal. The major defects observed include impaired ventricular myocardial differentiation, the ectopic appearance of cell masses in the AV cushion, the right-shifted interventricular septum (IVS) and impaired myocardium of the AV canal. However, the fates of the endocardium and myocardium were not disrupted in NICD1-activated hearts. One of the Notch target genes, Hesr1, was found to be strongly induced in both the ventricle and the AV canal of NICD1-activated hearts. However, a knockout of the Hesr1 gene from NICD-activated hearts rescues only the abnormality of the AV myocardium. We searched for addnl. possible targets of NICD1 activation by GeneChip anal. and found that Wnt2, Bmp6, jagged 1 and Tnni2 are strongly upregulated in NICD1-activated hearts, and that the activation of these genes was also observed in the absence of Hesr1. Our present study thus indicates that the Notch1 signaling pathway plays a suppressive role both in AV myocardial differentiation and the maturation of the ventricular myocardium.
RE.CNT 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 6 OF 13 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN

AN 2006:586060 BIOSIS
DN PREV200600596686
TI Notch signaling pathway contributes to osteosarcoma growth, tumorigenesis and metastasis.
AU Zhang, Pingyu [Reprint Author]; Mobley, Aaron K.; Yang, Yanwen; Lee, Kenneth A.; Zweidler-Mckay, Patrick A.; Hughes, Dennis Pm
CS Univ Texas, MD Anderson Canc Ctr, Houston, TX 77030 USA
SO Proceedings of the American Association for Cancer Research Annual Meeting, (APR 2006) Vol. 47, pp. 633.
Meeting Info.: 97th Annual Meeting of the American-Association-for-Cancer-Research (AACR). Washington, DC, USA. April 01 -05, 2006. Amer Assoc Canc Res.
ISSN: 0197-016X.
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LA English
ED Entered STN: 8 Nov 2006
Last Updated on STN: 8 Nov 2006

L3 ANSWER 7 OF 13 CAPLUS COPYRIGHT 2008 ACS on STN DUPLICATE 4
AN 2005:713955 CAPLUS
DN 143:187909
TI Methods of using databases to create gene-expression microarrays, equine and canine microarrays created thereby, and uses of the microarrays
IN Bertone, Alicia; Gu, Weisong
PA The Ohio State University, USA
SO PCT Int. Appl., 1475 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2005067649	A2	20050728	WO 2005-XA517	20050107

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MR, NE, SN, TD, TG
WO 2005067649 A2 20050728 WO 2005-US517 20050107
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
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MR, NE, SN, TD, TG
PRAI US 2004-535111P P 20040108
WO 2005-US517 A 20050107
AB Methods of preparing biol. databases, and databases prepared according to those
methods. The methods can be performed entirely using computer resources,
relying solely on publicly available biol. sequence information, and can
be used to generate species-specific nucleic acid microarrays. The
approach involves two major steps: identification of the 3' coding domains
(CDSs) and 3' expressed sequence tags (ESTs) in public domain sequence
databases and subsequent annotation of the sequences. For the algorithm
using 20,022 equine sequences in GenBank (June, 2003), the 3' equine CDSs

are identified by selecting the full and partial CDSs that have a stop codon at the 3' end. This approach ensures that sequences selected are anchored to the 3' end; most contain the 3' untranslated region (UTR), which is more species-specific, compared with the coding region. Use of the UTR sequence in probe design is an asset for improvement of microarray accuracy. An algorithm analyzes the partial equine CDSs and ESTs with those in a human-mouse CDS database (a subset of the GenBank nonredundant database) in order to provide annotation to the selected 3' equine sequences. A total of 3099 equine 3' coding sequences and 3' ESTs are selected for the equine-specific gene expression array, and 68,266 oligonucleotide probes designed according to Affymetrix's chip design guide. Microarray anal. identified genes expressed in equine synoviocytes in the absence and presence of lipopolysaccharide, as well as differentially expressed genes in developmental orthopedic disease (osteochondrosis desiccans and cervical vertebral malformation), equine osteoarthritis, equine protozoal myelitis, herpes virus-1 infection, potentially compromising stress, and laminitis in horses. Analogous methods are used to generate a canine-specific microarray to detect gene expression during osteoarthritis in dogs. [This abstract record is one of two records for this document necessitated by the large number of index entries required to fully index the document and publication system constraints.].

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AN 2005414857 EMBASE

TI Hesr, a mediator of the motch signaling, functions in heart and vessel development.

AU Kokubo, Hiroki, Dr. (correspondence)

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AU Miyagawa-Tomita, Sachiko
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AU Johnson, Randy L.
CS Department of Biochemistry and Molecular Biology, MD Anderson Cancer
Center, Houston, TX 77030-4095, United States.
SO Trends in Cardiovascular Medicine, (Jul 2005) Vol. 15, No. 5, pp. 190-194.
Refs: 33
ISSN: 1050-1738 CODEN: TCMDEQ
PUI S 1050-1738(05)00059-9
CY United States
DT Journal; General Review; (Review)
FS 002 Physiology
021 Developmental Biology and Teratology
029 Clinical and Experimental Biochemistry
LA English
SL English
ED Entered STN: 13 Oct 2005
Last Updated on STN: 13 Oct 2005
AB Hesr genes are members of the hairy and enhancer of split-related (hesr)
gene family of basic helix-loop-helix-type transcriptional repressors.
hesr genes have been implicated in cardiovascular development as the
primary targets of Notch signaling. Functional analysis of hesr2 knockout
mice revealed abnormal cardiac hemodynamics, such as atrioventricular
valve regurgitation and reduced left ventricular systolic function, caused
by hypoplastic AV valves and abnormal cardiomyocytes. Recent evidence
demonstrates that hesr1 and hesr2 function redundantly in
epithelial-to-mesenchymal transformation during atrioventricular valve
formation and maintenance of trabecular cells in the heart ventricles, and
in arterial-venous differentiation of blood vessels. This review
highlights the many functions of the hesr gene family in heart and vessel
development. .COPYRGT. 2005, Elsevier Inc.

L3 ANSWER 9 OF 13 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
DUPLICATE 5

AN 2004:244930 BIOSIS
DN PREV200400246625
TI Synergy and antagonism between Notch and BMP receptor signaling pathways
in endothelial cells.
AU Itoh, Fumiko; Itoh, Susumu; Goumans, Marie-Jose; Valdimarsdottir, Gudrun;
Iso, Tatsuya; Dotto, G. Paolo; Hamamori, Yasuo; Kedes, Larry; Kato,
Mitsuyasu; ten Dijke, Peter [Reprint Author]
CS Division of Cellular Biochemistry, Netherlands Cancer Institute,
Plesmanlaan 121, 1066 CX, Amsterdam, Netherlands
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SO EMBO (European Molecular Biology Organization) Journal, (11 February 2004)
Vol. 23, No. 3, pp. 541-551. print.
ISSN: 0261-4189 (ISSN print).
DT Article
LA English
ED Entered STN: 6 May 2004
Last Updated on STN: 6 May 2004
AB Notch and bone morphogenetic protein signaling pathways are important for cellular differentiation, and both have been implicated in vascular development. In many cases the two pathways act similarly, but antagonistic effects have also been reported. The underlying mechanisms and whether this is caused by an interplay between Notch and BMP signaling is unknown. Here we report that expression of the Notch target gene, Herp2, is synergistically induced upon activation of Notch and BMP receptor signaling pathways in endothelial cells. The synergy is mediated via RBP-Jkappa/CBF-1 and GC-rich palindromic sites in the Herp2 promoter, as well as via interactions between the Notch intracellular domain and Smad that are stabilized by p/CAF. Activated Notch and its downstream effector Herp2 were found to inhibit endothelial cell (EC) migration. In contrast, BMP via upregulation of Id1 expression has been reported to promote EC migration. Interestingly, Herp2 was found to antagonize BMP receptor/Id1-induced migration by inhibiting Id1 expression. Our results support the notion that Herp2 functions as a critical switch downstream of Notch and BMP receptor signaling pathways in ECs.

L3 ANSWER 10 OF 13 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on
STN DUPLICATE 6
AN 2004:274686 BIOSIS
DN PREV200400275095
TI Expression of serotonin receptors and role of serotonin in human prostate
cancer tissue and cell lines.
AU Dizeyi, N. [Reprint Author]; Bjartell, A.; Nilsson, E.; Hansson, J.;
Gadaleanu, V.; Cross, N.; Abrahamsson, P.-A.
CS Malmo Univ HospDept Urol, Univ Lund, Lund, Sweden
Nishtman.dizeyi@urokir.lu.se
SO Prostate, (May 15 2004) Vol. 59, No. 3, pp. 328-336. print.
ISSN: 0270-4137 (ISSN print).
DT Article
LA English
ED Entered STN: 2 Jun 2004
Last Updated on STN: 2 Jun 2004
AB BACKGROUND. Increase in the number of serotonin (5-HT) releasing
neuroendocrine (NE) cells has been shown to be correlated with tumor
progression, loss of androgen dependence, and poor prognosis. Serotonin
is a well-known mitogen which mediates a wide variety of physiological
effects via multiple receptors, of which receptor subtype 1 (5-
HTR1) has been identified in prostate cancer (PC) cell lines.
Recently, 5-HT has been found to show growth-promoting activity and to be
functionally related to oncogenes. MATERIALS AND METHODS. Localization,
protein content, and mRNA expression of 5-HTR subtype 1A, 1B, and 1D was
studied in prostatic tissue (35 patients), metastases, PC cell lines, a
benign prostatic stromal cell line (human prostate cell preparation
(hPCP)), and xenografts of PC-3 cells by immunohistochemistry (IHC),
Western blotting, and RT-PCR, respectively. The growth-inhibition effect
of a 5-HT1A antagonist (NAN-190) on PC cell lines was studied using a
bromodeoxyuridine (BrdU) assay. RESULTS. A strong immunoreaction of
5-HTR1A and 113 was demonstrated in high-grade tumor cells (35/35) and a
small number of BPH cells, whereas 5-HTR1D was confined to vascular
endothelial cells. 5-HTR1A was also demonstrated in PC cells metastasized

to lymph node and bone, PC-3, DU145, LNCaP, and in xenografts of PC-3 cells and hPCP. Western blot analysis gave strong bands from PC tissue extracts compared to BPH tissue. Using RT-PCR, 5-HTR1A mRNA was demonstrated in all PC cell lines. An antagonist of 5-HTR1A (NAN-190) inhibited the growth of PC-3, DU145, and LNCaP cells but not of hPCP cells. CONCLUSIONS. This is the first study demonstrating an overexpression of 5-HTR subtypes 1A and 1 B in PC cells, especially in high-grade tumors. Moreover, 5-HT stimulates proliferation of PC cells and 5-HTR1A antagonists inhibit proliferation. Thus, we propose that 5-HT has an important role in tumor progression, especially in the androgen-independent state of the disease. The design of specific antagonists for this type of receptor might be useful for the growth control of androgen-independent tumors. Copyright 2004 Wiley-Liss. Inc.

L3 ANSWER 11 OF 13 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2003:656915 CAPLUS
DN 139:191426
TI Modulation of stem cell differentiation using inhibitory RNAs to control gene expression
IN Andrews, Peter; Walsh, James; Gokhale, Paul
PA Axordia Limited, UK
SO PCT Int. Appl., 157 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003068961	A2	20030821	WO 2003-GB579	20030212
WO 2003068961	A3	20040318		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,

PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ,
UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF,
BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
AU 2003214363 A1 20030904 AU 2003-214363 20030212
EP 1474512 A2 20041110 EP 2003-709933 20030212
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
US 20050202428 A1 20050915 US 2005-504173 20050422
US 20070087991 A1 20070419 US 2006-600125 20061116
PRAI GB 2002-3359 A 20020213
GB 2002-3387 A 20020213
WO 2003-GB579 W 20030212
US 2005-504173 B1 20050422
AB The invention relates to a method to modulate stem cell differentiation
comprising introducing inhibitory RNA (RNAi) into a stem cell to ablate
mRNA's which encode polypeptides which are involved in stem cell
differentiation; RNAi mols., DNA mols. encoding said RNAi mols.; and cells
obtained by said method. Specifically, iRNA against a range of receptors,
such as Enhancer of split receptors, involved in signal transduction in
differentiation are targeted. Differentiation-specific transcription
factor genes may also be targeted.

L3 ANSWER 12 OF 13 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on
STN DUPLICATE 7
AN 2003:564736 BIOSIS
DN PREV200300566585
TI Enhanced gene activation by Notch and BMP signaling cross-talk.
AU Takizawa, Takumi; Ochiai, Wataru; Nakashima, Kinichi; Taga, Tetsuya
[Reprint Author]
CS Department of Cell Fate Modulation, Institute of Molecular Embryology and

Genetics, Kumamoto University, Kumamoto, 860-0811, Japan
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SO Nucleic Acids Research, (October 1 2003) Vol. 31, No. 19, pp. 5723-5731.
print.
ISSN: 0305-1048 (ISSN print).
DT Article
LA English
ED Entered STN: 3 Dec 2003
Last Updated on STN: 3 Dec 2003
AB The signaling systems of Notch and bone morphogenetic protein (BMP) are highly conserved from flies to mammals and have been shown to be important in the development of multiple organs. For instance, in the fate determination of mouse neuroepithelial cells, Notch signaling plays a role in keeping the progenitors from differentiating into neurons. BMP is also known to inhibit neuronal differentiation. In this paper, we show that BMP2 enhances Notch-induced transcriptional activation of Hes-5 and Hesr-1 in mouse neuroepithelial cells. BMP2 stimulation, in addition to the introduction of the intracellular domain of Notch (NIC), resulted in enhanced activation of the Hes-5 gene promoter. RBP-Jkappa binding to its target sequence is important not only for Notch signaling, but also for BMP2 signaling, to activate the Hes-5 gene promoter. Smad1, a Smad species that is activated by BMP2, barely interacted with NIC, but did form a complex with NIC in the simultaneous presence of the coactivators P/CAF and p300. Recruitment of p300 to the NIC-containing complex was facilitated by activated Smad1, which is suggested to contribute to BMP2-mediated enhancement of Notch-induced Hes-5 expression. These data suggest a novel functional cooperation between Notch signaling and BMP signaling.

L3 ANSWER 13 OF 13 CAPLUS COPYRIGHT 2008 ACS on STN DUPLICATE 8
AN 2003:555758 CAPLUS
DN 139:286763
TI Gene array analysis of bone morphogenetic protein type I receptor-induced osteoblast differentiation
AU Korchynskyi, Olexander; Dechering, Koen J.; Sijbers, Anneke M.; Olijve,

Wiebe; Ten Dijke, Peter
CS Division of Cellular Biochemistry, The Netherlands Cancer Institute,
Amsterdam, Neth.
SO Journal of Bone and Mineral Research (2003), 18(7), 1177-1185
CODEN: JBMREJ; ISSN: 0884-0431
PB American Society for Bone and Mineral Research
DT Journal
LA English
AB The genomic response to BMP was investigated by ectopic expression of activated BMP type I receptors in C2C12 myoblast using cDNA microarrays. Novel BMP receptor target genes with possible roles in inhibition of myoblast differentiation and stimulation of osteoblast differentiation were identified. Bone morphogenetic proteins (BMPs) have an important role in controlling mesenchymal cell fate and mediate these effects by regulating gene expression. BMPs signal through three distinct specific BMP type I receptors (also termed activin receptor-like kinases) and their downstream nuclear effectors, termed Smads. The critical target genes by which activated BMP receptors mediate change cell fate are poorly characterized. We performed transcriptional profiling of C2C12 myoblasts differentiation into osteoblast -like cells by ectopic expression of three distinct constitutively active (ca)BMP type I receptors using adenoviral gene transfer. Cells were harvested 48 h after infection, which allowed detection of both early and late response genes. Expression anal. was performed using the mouse GEM1 microarray, which is comprised of approx. 8700 unique sequences. Hybridizations were performed in duplicate with a reverse fluor labeling. Genes were considered to be significantly regulated if the p value for differential expression was less than 0.01 and inverted expression ratios per duplicate successful reciprocal hybridizations differed by less than 25%. Each of the three caBMP type I receptors stimulated equal levels of R-Smad phosphorylation and alkaline phosphatase activity, an early marker for osteoblast differentiation. Interestingly, all three type I receptors induced identical transcriptional profiles; 97 genes were

significantly upregulated and 103 genes were downregulated. Many extracellular matrix genes were upregulated, muscle-related genes downregulated, and transcription factors/signaling components modulated.
In addition to 41 expressed sequence tags without known function and a number of known BMP target genes, including PPAR-γ and fibromodulin, a large number of novel BMP target genes with an annotated function were identified, including transcription factors HesR1, ITF-2, and ICSBP, apoptosis mediators DRP-1 death kinase and ZIP kinase, IκBα, Edg-2, ZO-1, and E3 ligase Dactylin. These target genes, some of them unexpected, offer new insights into how BMPs elicit biol. effects, in particular into the mechanism of inhibition of myoblast differentiation and stimulation of osteoblast differentiation.
RE.CNT 60 THERE ARE 60 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

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FULL ESTIMATED COST	0.48	53.67

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CA SUBSCRIBER PRICE	0.00	

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=> s hesr1 or htr1 or herp2 or hesr 1 or hey1 or hey 1
L4 451 HESR1 OR HTR1 OR HERP2 OR HESR 1 OR HEY1 OR HEY 1

=> s l4 (3a) human
L5 51 L4 (3A) HUMAN

=> s l5 and (mouse or murine)
L6 19 L5 AND (MOUSE OR MURINE)

=> dup rem l6
PROCESSING COMPLETED FOR L6
L7 11 DUP REM L6 (8 DUPLICATES REMOVED)

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L7 ANSWER 1 OF 11 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
AN 2008:324661 BIOSIS
DN PREV200800324660
TI Microarray analysis of freshly-microdissected intact human dermal papilla
identified upregulation of genes that could contribute to biological
distinctiveness.
AU Ohyama, M. [Reprint Author]; Shimizu, A.; Kobayashi, T.; Amagai, M.
CS Keio Univ, Tokyo, Japan
SO Journal of Investigative Dermatology, (APR 2008) Vol. 128, No. Suppl. 1,
pp. S147.
Meeting Info.: International Investigative Dermatology Meeting. Kyoto,
JAPAN. May 14 -17, 2008. Japanese Soc Investigat Dermatol; Soc Investigat
Dermatol; European Soc Dermatol Res; Federat Pharmaceut Manufactures Assoc
Japan; Galderma; Janssen Pharmaceut KK; Maruho Co Ltd; Sanofi Aventis KK;
Torii Pharmaceut Co Ltd; Abbott Japan Co Ltd; CERIES; Chanel; Clin Labs
KK; Dainippon Sumitomo Pharma; Eisai Co Ltd; GlaxoSmithKline KK; Kyowa

Hakko Kogyo Co Ltd; Mistubishi Tanabe Pharma Corp; Nippon Boehringer
Ingelheim; Novartis Pharma KK; Schering Plough; Shionogi & Co Ltd;
Shiseido Co Ltd; Japan Cosmet Ind Assoc; Igaku Shoin; Pierre Fabre Japan
Co Ltd.
CODEN: JIDEAE. ISSN: 0022-202X.
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LA English
ED Entered STN: 29 May 2008
Last Updated on STN: 29 May 2008

L7 ANSWER 2 OF 11 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
AN 2008:2534 BIOSIS
DN PREV200800003251
TI gamma-secretase inhibitor prevents Notch3 activation and reduces proliferation in human lung cancers.
AU Konishi, Jun; Kawaguchi, Keiko S.; Vo, Huan; Haruki, Nobuhiro; Gonzalez,
Adriana; Carbone, David P.; Dang, Thao P. [Reprint Author]
CS Vanderbilt Ingram Canc Ctr, 658 PRB, Nashville, TN 37232 USA
thao.p.dang@vanderbilt.edu
SO Cancer Research, (SEP 1 2007) Vol. 67, No. 17, pp. 8051-8057.
CODEN: CNREA8. ISSN: 0008-5472.
DT Article
LA English
ED Entered STN: 12 Dec 2007
Last Updated on STN: 12 Dec 2007
AB Notch receptors are key regulators of development by controlling cell-fate
determination in many multicellular organisms. Genes that are important
for normal differentiation play a role in cancer when their normal
functions became dysregulated. Notch signaling has been shown to promote
and maintain survival of many types of cancers, and we previously have
shown that Notch3 plays an important role in lung cancer. In this study,
we showed that a high percentage of lung cancer lines expressed Jagged1,
Notch receptors, and their transcriptional target genes (HES1, Hey1),
suggesting that the Notch pathway plays an important role in lung cancer
biology. Thus, inhibition of Notch receptor activation represents a
compelling treatment strategy. Notch activation requires proteolytic

cleavage of the receptor by gamma-secretase protein complex. In this study, we determined the ability of MRK-003, a gamma-secretase inhibitor, to inhibit Notch3 signaling, growth, and apoptosis of lung cancer cell lines in vitro and in vivo using mouse xenograft models. We also found that MRK-003 inhibited Notch3 signaling, reduced tumor cell proliferation, inhibited serum independence, and induced apoptosis. This drug had no effect when Notch3 expression was knocked down using small interfering RNA (siRNA), suggesting that the observed effects were mediated by specific action on this receptor. In conclusion, these results support the hypothesis that inhibition of Notch activation using gamma-secretase inhibitor represents a potential new approach for the targeted therapy of lung cancer.

L7 ANSWER 3 OF 11 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
AN 2007:472499 BIOSIS
DN PREV200700470038
TI Integrative genomic analyses on HES/HEY family: Notch-independent HES1, HES3 transcription in undifferentiated ES cells, and Notch-dependent HES1, HES5, HEY1, HEY2, HEYL transcription in fetal tissues, adult tissues, or cancer.
AU Katoh, Masuko; Katoh, Masaru [Reprint Author]
CS Natl Canc Ctr, Res Inst, Genet and Cell Biol Sect, Chuo Ku, 5-1-1 Tsukiji, Tokyo 1040045, Japan
mkatoh-kkr@umin.ac.jp
SO International Journal of Oncology, (AUG 2007) Vol. 31, No. 2, pp. 461-466.
ISSN: 1019-6439.
DT Article
LA English
ED Entered STN: 5 Sep 2007
Last Updated on STN: 20 Sep 2007
AB Notch signaling pathway maintains stem cells through transcriptional activation of HES/HEY family members to repress tissue-specific transcription factors. Here, comparative integromic analyses on HES/HEY family members were carried out. HES3 gene encodes two isoforms due to

alternative promoters. Complete coding sequence of HES3 variant 2 was determined by curating CX755241.1 EST. Refined phylogenetic analysis using HES3 variant 2 instead of variant 1 revealed that mammalian bHLH transcription factors with Orange domain were grouped into HES subfamily (HES 1, HES2, HES3, HES4, HES5, HES6, HES7) and HEY subfamily (HEY1, HEY2, HEYL, HESL/HELT, DEC1/ BHLHB2, DEC2/BHLHB3). Eight amino-acid residues were added to the C-terminal WRPW motif in human HES3 due to lineage specific T to G nucleotide change at stop codon of chimpanzee, rat, and mouse HES3 orthologs. HES1 and HES3 were expressed in undifferentiated embryonic stem (ES) cells. HES1 was also expressed in fetal tissues, and regenerating liver. HES1, HEY1 and HEY2 were expressed in endothelial cells. HES1, HES4 and HES6 were expressed in gastric cancer, HES1 and DEC1 in pancreatic cancer, HES1, HES2, HES4, HES6 and DEC2 in colorectal cancer. HES6 was also expressed in other tumors, such as brain tumors, melanoma, small cell lung cancer, retinoblastoma, ovarian cancer, and breast cancer. Double NANOG-binding sites, CSL/ RBPSUH-binding, site and TATA-box in HES1 promoter,NANOG-, SOX2-, POU5F1/OCT3/OCT4-binding sites and TATA-box in HES3 promoter, double CSL-binding sites in HES5 promoter, SOX2-, POU-binding sites and TATA-box in HES6 promoter, and CSL-binding site in HEY1, HEY2 and HEYL promoters were evolutionarily conserved. However, double CSL-binding sites in mouse Hes7 promoter were not conserved in human HES7 promoter. Together these facts indicate that HES1 and HES3 were target genes of the ES cell-specific network of transcription factors, and that HES1, HES5, HEY1, HEY2 and HEYL were target genes of Notch signaling pathway.

L7 ANSWER 4 OF 11 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
AN 2006:236950 BIOSIS
DN PREV200600238930
TI Comparative genomics on HHIP family orthologs.
AU Katoh, Yuriko; Katoh, Masaru [Reprint Author]

CS Natl Canc Ctr, Res Inst, Genet and Cell Biol Sect, Chuo Ku, 5-1-1 Tsukiji,
Tokyo 1040045, Japan
mkatoh@ncc.go.jp
SO International Journal of Molecular Medicine, (FEB 2006) Vol. 17, No. 2,
pp. 391-395.
ISSN: 1107-3756.
DT Article
LA English
OS GenBank-NP071920.1; EMBL-NP071920.1; DDJB-NP071920.1; GenBank-NM032425.3;
EMBL-NM032425.3; DDJB-NM032425.3; GenBank-NM024746.2; EMBL-NM024746.2;
DDJB-NM024746.2; GenBank-NP079022.1; EMBL-NP079022.1; DDJB-NP079022.1;
GenBank-NM020259.3; EMBL-NM020259.3; DDJB-NM020259.3; GenBank-NM030175.1;
EMBL-NM030175.1; DDJB-NM030175.1; GenBank-AC107504.4; EMBL-AC107504.4;
DDJB-AC107504.4; GenBank-AC094820.6; EMBL-AC094820.6; DDJB-AC094820.6;
GenBank-AC134264.2; EMBL-AC134264.2; DDJB-AC134264.2
ED Entered STN: 19 Apr 2006
Last Updated on STN: 19 Apr 2006
AB Hedgehog, FGF, VEGF, and Notch signaling pathways network together for
vascular remodeling during embryogenesis and carcinogenesis. HHIP1 (HHIP)
is an endogenous antagonist for SHH, IHH, and DHH. Here, comparative
integromics analyses on HHIP family members were performed by using
bioinformatics and human intelligence. HHIP1, HHIP2 (HHIPL1 or KIAA1822)
and HHIP3 (HHIPL2 or KIAA1822L) constitute human HHIP gene family. Rat
Hhip1, Hhip2, and Hhip3 genes were identified within AC107504.4,
AC094820.6, and AC134264.2 genome sequences, respectively.
HHIP-homologous (HIPH) domain with conserved 18 Cys residues was
identified as the novel domain conserved among mammalian HHIP1, HHIP2, and
HHIP3 orthologs. HHIP1 mRNA was expressed in coronary artery endothelial
cells, prostate, and rhabdomyosarcoma. HHIP2 mRNA was expressed in
trabecular bone cells. HHIP3 mRNA was expressed in testis, thyroid gland,
osteoarthritic cartilarge, pancreatic cancer, and lung cancer. Promoters
of HHIP family genes were not well conserved between human and rodents.

Although GLI-, CSL-, and HES/HEY-binding sites were not identified, eleven bHLH-binding sites were identified within human HHIP1 promoter. Expression of HES/ HEY family members, including HES1, HES2, HES3, HES4, HES5, HES6, HES7, HEY1, HEY2 and HEYL, in coronary artery endothelial cells was not detected in silico. Up-regulation of HHIP1 due to down-regulation of Notch-CSL-HES/HEY signaling cascade repressing bHLH transcription factors results in down-regulation of the Hedgehog-VEGF-Notch signaling cascade. On the other hand, down-regulation of HHIP1 due to up-regulation of Notch signaling in vascular endothelial cells during angiogenesis results in up-regulation of the Hedgehog-VEGF-Notch signaling cascade. Because HHIP1 is the key molecule for vascular remodeling, HHIP1 is the pharmacogenomics target in the fields of oncology and vascular medicine.

L7 ANSWER 5 OF 11 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
DUPLICATE 1
AN 2006:249368 BIOSIS
DN PREV200600245147
TI Notch signaling is required for normal prostatic epithelial cell proliferation and differentiation.
AU Wang, Xi-De; Leow, Ching Ching; Zha, Jiping; Tang, Zhijun; Modrusan, Zora; Radtke, Freddy; Aguet, Michel; de Sauvage, Frederic J.; Gao, Wei-Qiang [Reprint Author]
CS Genentech Inc, Dept Mol Biol, 1 DNA Way, San Francisco, CA 94080 USA
gao@gene.com
SO Developmental Biology, (FEB 1 2006) Vol. 290, No. 1, pp. 66-80. CODEN: DEBIAO. ISSN: 0012-1606.
DT Article
LA English
ED Entered STN: 26 Apr 2006
Last Updated on STN: 26 Apr 2006
AB Notch pathway is crucial for stem/progenitor cell maintenance, growth and differentiation in a variety of tissues. Using a transgenic cell ablation approach, we found in our previous study that cells expressing Notch 1 are crucial for prostate early development and re-growth. Here, we further define the role of Notch signaling in regulating prostatic epithelial cell

growth and differentiation using biochemical and genetic approaches in ex vivo or in vivo systems. Treatment of developing prostate grown in culture with inhibitors of gamma-secretase/presenilin, which is required for Notch cleavage and activation, caused a robust increase in proliferation of epithelial cells co-expressing cytokeratin 8 and 14, lack of luminal/basal layer segregation and dramatically reduced branching morphogenesis. Using conditional Notch1 gene deletion mouse models, we found that inactivation of Notch1 signaling resulted in profound prostatic alterations, including increased tufting, bridging and enhanced epithelial proliferation. Cells within these lesions co-expressed both luminal and basal cell markers, a feature of prostatic epithelial cells in predifferentiation developmental stages. Microarray analysis revealed that the gene expression in a number of genetic networks was altered following Notch1 gene deletion in prostate. Furthermore, expression of Notch1 and its effector Hey-1 gene in human prostate adenocarcinomas were found significantly down-regulated compared to normal control tissues. Taken together, these data suggest that Notch signaling is critical for normal cell proliferation and differentiation in the prostate, and deregulation of this pathway may facilitate prostatic tumorigenesis.

L7 ANSWER 6 OF 11 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
AN 2005:395802 BIOSIS
DN PREV200510185834
TI Hey1, a direct Notch target gene, is up-regulated by BMP-2 and reduces osteoblast matrix mineralization and Cbfa1/Runx2 transcriptional activity.
AU Susa, Mira [Reprint Author]; Zamurovic, Natasa; Cappellen, David; Rohner, Daisy
CS Novartis Inst Biomed Res, Basel, Switzerland
SO FASEB Journal, (MAY 14 2004) Vol. 18, No. 8, Suppl. S, pp. C158. Meeting Info.: Annual Meeting of the American-Society-for-Biochemistry-and-Molecular-Biology/8th Congress of the International-Union-for-Biochemistry-

and-Molecular-Biology. Boston, MA, USA. June 12 -16, 2004. Amer Soc
BioChem & Mol Biol; Int Union Biochem & Mol Biol.
CODEN: FAJOEC. ISSN: 0892-6638.
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LA English
ED Entered STN: 5 Oct 2005
Last Updated on STN: 5 Oct 2005
AB To examine early events in osteoblast differentiation, we analyzed the
expression of about 9,400 genes in the murine MC3T3 cell line, whose robust differentiation was documented cytochemically and molecularly. The cells were stimulated for I and 3 days with the osteogenic stimulus containing bone morphogenetic protein 2 (BMP-2).
Total RNA was extracted and analyzed by Affymetrix GeneChipoligonucleotide
arrays. A regulated expression of 3 94 known genes and 295 expressed
sequence tags (EST) was detected. The sensitivity and reliability of
detection by microarrays was shown by confirming the expression pattern
for 20 genes by radioactive quantitative RT-PCR. Functional classification of regulated genes was performed, defining the groups of
regulated Growth Factors, Receptors and Transcription Factors. The most
interesting finding was concomitant activation of TGF-beta, Writ and Notch
signaling pathways, confirmed by strong up-regulation of their target
genes by PCR. TGF-beta pathway is activated by stimulated production of
the growth factor itself, while mechanism of Writ and Notch activation
remains elusive. We showed BMP-2 stimulated expression of Hey1, a direct
Notch target gene, in mouse C2C12 cells, human mesenchymal cells and mouse calvaria. SiRNA-mediated inhibition of Hey1 induction led to an increase in osteoblast matrix mineralization, suggesting that
Hey1 is a negative regulator of osteoblast maturation. This negative
regulation is apparently achieved via interaction with Cbfa1/Runx2: Hey1
completely abrogated Cbfa1/Runx2 transcriptional activity. These findings
identify Notch-Hey1 pathway as a negative regulator of osteoblast differentiation/maturation, which is a completely novel aspect of osteogenesis.

L7 ANSWER 7 OF 11 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
AN 2004:123422 BIOSIS
DN PREV200400116703
TI Fetal liver stem/progenitor cells specific genes.
AU Goetz, David [Reprint Author]; Bottinger, Erwin [Reprint Author];
Shafritz, David A. [Reprint Author]; Petkov, Petko M. [Reprint Author];
Zavadil, Jiri [Reprint Author]; Grozdanov, Petar N. [Reprint Author];
Dabeva, Mariana D. [Reprint Author]
CS Albert Einstein College of Medicine, Bronx, NY, USA
SO Hepatology, (October 2003) Vol. 38, No. 4 Suppl. 1, pp. 290A. print.
Meeting Info.: 54th Annual Meeting of the American Association for the
Study of Liver Diseases. Boston, MA, USA. October 24-28, 2003. American
Association for the Study of Liver Diseases.
ISSN: 0270-9139 (ISSN print).
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
Conference; (Meeting Poster)
LA English
ED Entered STN: 3 Mar 2004
Last Updated on STN: 3 Mar 2004
AB n order to identify new and differentially expressed genes in fetal rat
liver that are specific for epithelial stem/progenitor cells and genes
involved in liver progenitor cell differentiation, we used murine
cDNA microarrays containing 8,976 cDNAs, available at the Functional
Genomic Facility, AECOM. The expression pattern of fetal liver
stem/progenitor cells was studied from embryonic day 13 through birth, 7
days after birth and in adult liver. The driver RNAs were isolated from
cells adhered to the dish after plating the cell suspension in order to
remove the blood cells. Reference RNA was isolated from the livers of
newborn rats. We found that 511 genes present on the cDNA microarrays
were developmentally regulated. These genes fall in two major
hierarchical clusters, according to their pattern of expression. The 281
genes that are down-regulated during fetal liver development were
distributed in functional groups and further analyzed. In this study,
special attention was paid to genes that were induced in fetal liver but

were not expressed (or expressed at a very low level) in adult liver.

These genes are of special interest because they can serve as specific markers for identification and for isolation of liver stem/progenitor cells. In addition, these genes represent links to understanding the fetal liver specific molecular pathways that govern cell proliferation, survival, apoptosis and differentiation. To determine which of the 281 over-expressed genes in 13-14 day fetal liver that are down-regulated in adult liver are progenitor cells specific, we searched in the available databases whether the expression of these genes in adult liver was previously reported. Seventy genes were further analyzed: the clones of interest were hybridized to radioactive labeled 32P cDNA synthesized from fetal and adult liver RNAs. For 48 of the clones, we found that there was little or no expression in adult liver. The expression level of 25 selected clones was analyzed further by quantitative PCR, and they were confirmed as highly induced in fetal hepatoblasts compared to adult liver.

Half of the 48 clones are ESTs. The known genes fall in different categories, the major four being: genes related to transcription; signal transduction; morphogenesis, histogenesis and organogenesis; cell adhesion, de-adhesion and migration. Some of the known genes over-expressed in fetal liver that are not expressed or expressed at very low level in adult liver are: Grb10 (AA260248), Fhl2 (AA023645), Tnc (AA270625), Peg3 (AA003064), Hey1 (AA049474), Enah ((AA217593), Pkcd (AA276844), Lox (W96914), Shcbp1 (AA265225), Magoh (AA254528), Manba (AA200473), Klf5 (AA432818), Gpc3 (AA274932), Pcolce2 (AA153907), Ppap2c (AA220316), Nfkb2 (AA060802), Adam19 (AA051790), Akap12 (AA387076), Tagln (BC003795. It should be noted, that most of the 48 clones and all those listed here that we have identified as liver progenitor cells specific,

are expressed in stem cells of embryonic, hematopoietic, or mesenchymal origin. Two of the presented genes encode cell surface proteins: a disintegrin and metalloproteinase domain 19 (Adam19) (meltrin beta), glypican 3. Using in situ hybridization, we are currently verifying whether our putative liver progenitor cell specific genes are expressed in hepatoblasts and in rare progenitor cells that remain in the adult liver. Identifying and cloning new genes that are expressed uniquely in liver stem/progenitor cells will allow us to design a method for isolation of these cells and to study their role in liver development, growth control and regeneration.

L7 ANSWER 8 OF 11 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
DUPLICATE 2
AN 2000:452682 BIOSIS
DN PREV200000452682
TI Comparative analysis of the human and mouse Hey1 promoter: Hey genes are new notch target genes.
AU Maier, Manfred M.; Gessler, Manfred [Reprint author]
CS Physiologische Chemie I, Biozentrum der Universitaet Wuerzburg, Am Hubland, 97074, Wuerzburg, Germany
SO Biochemical and Biophysical Research Communications, (August 28, 2000) Vol. 275, No. 2, pp. 652-660. print.
CODEN: BBRCA9. ISSN: 0006-291X.
DT Article
LA English
ED Entered STN: 25 Oct 2000
Last Updated on STN: 10 Jan 2002
AB Hey genes (Hey1, Hey2 and HeyL) encode a new group of basic helix-loop-helix transcription factors that are related to the hairy/Enhancer of split genes. In the present study, we cloned and characterized the promoter region of the human and mouse Hey1 gene. The transcription initiation site was located 138 nucleotides upstream of the start codon. There is a minimal sequence element (nt -30 to -247) that is essential and important for basal transcription in three different cell types. Further upstream, a highly conserved sequence block (nt -324 to -646; apprx90% human/mouse

similarity) could be identified that contains several putative binding sites for transcription factors and likely represents an important regulatory region for this gene. Cotransfection experiments demonstrated that the mHey1 promoter activity is up-regulated by the activated form of all four mammalian Notch receptors via two functional RBP-Jkappa binding sites. The other members of the Hey gene family, Hey2 and HeyL, also possess RBP-Jkappa binding sites and they are similarily responsive to Notch signaling. Thus, our data clearly demonstrate that Hey genes form a new class of Notch signal transducers that should prove to be relevant in various developmental processes.

L7 ANSWER 9 OF 11 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
DUPLICATE 3
AN 2000:346818 BIOSIS
DN PREV200000346818
TI Characterization of the human and mouse HEY1 , HEY2, and HEYL genes: Cloning, mapping, and mutation screening of a new bHLH gene family.
AU Steidl, C.; Leimeister, C.; Klamt, B.; Maier, M.; Nanda, I.; Dixon, M.; Clarke, R.; Schmid, M.; Gessler, M. [Reprint author]
CS Physiologische Chemie I, Theodor-Boveri-Institut, Biozentrum der Universitaet Wuerzburg, Am Hubland, D-97074, Wuerzburg, Germany
SO Genomics, (June, 2000) Vol. 66, No. 2, pp. 195-203. print.
CODEN: GNMCEP. ISSN: 0888-7543.
DT Article
LA English
OS Genbank-AJ243895; EMBL-AJ243895; Genbank-AJ249545; EMBL-AJ249545; Genbank-AJ271867; EMBL-AJ271867; Genbank-AJ271868; EMBL-AJ271868; Genbank-AJ272214; EMBL-AJ272214; Genbank-AJ272215; EMBL-AJ272215
ED Entered STN: 16 Aug 2000
Last Updated on STN: 7 Jan 2002
AB Many basic helix-loop-helix (bHLH) transcription factors are known as key regulators of embryonic development or differentiation in various species.
We have isolated and characterized three new hairy-related bHLH transcription factor genes from mouse and human (hairy and Enhancer-of-split related with YRPW motif; HEY1, HEY2, and HEYL). All three HEY genes have a similar genomic structure with five exons.

Together with a highly related Drosophila homologue, they form a new bHLH gene subfamily that is different from both hairy and the known vertebrate Hes and Her genes. While the overall structure with the bHLH domain, Orange domain, and WRPW motif is similar, the last motif is changed to KPYRPWG in Hey1/2 and absent in HeyL. This and other sequence features suggest Hey proteins to have unique functional properties. The genes were mapped by fluorescence in situ hybridization and RH mapping to the following human chromosomes: (HEY1) 8q21, (HEY2) 6q21, and (HEYL) 1p34.3. Based on expression patterns and map location, HEY genes are candidates for several human or mouse disease loci. However, initial screening of DNA from affected individuals for two human disorders and four mouse mutants did not reveal any diagnostic alterations in the coding regions.

L7 ANSWER 10 OF 11 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN DUPLICATE 4

AN 1999:358822 BIOSIS

DN PREV199900358822

TI Identification and expression of a novel family of bHLH cDNAs related to Drosophila hairy and enhancer of split.

AU Kokubo, Hiroki; Lun, Yi; Johnson, Randy L. [Reprint author]

CS Department of Biochemistry and Molecular Biology, University of Texas, MD Anderson Cancer Center, 1515 Holcombe Blvd., Houston, TX, 77030, USA

SO Biochemical and Biophysical Research Communications, (July 5, 1999) Vol. 260, No. 2, pp. 459-465. print.
CODEN: BBRCA9. ISSN: 0006-291X.

DT Article

LA English

OS Genbank-AF151521; EMBL-AF151521; DDBJ-AF151521; EMBL-AF151522; Genbank-AF151522; DDBJ-AF151522; EMBL-AF151523; Genbank-AF151523; DDBJ-AF151523

ED Entered STN: 2 Sep 1999
Last Updated on STN: 2 Sep 1999

AB In this report we describe the initial characterization of murine, human, and Drosophila hesr-1 (for hairy and enhancer of split related-1) a novel evolutionary conserved family of hairy/enhancer of split homologs. Hesr-1 cDNAs display features typical

of hairy and enhancer of split-type bHLH proteins including a N-terminal bHLH domain a conserved orange domain immediately C-terminal to the bHLH region. Despite their similarity to known hairy/enhancer of split homologs, hesr-1 cDNAs are divergent members of the hairy and enhancer of split bHLH family since the degree of sequence identity within the bHLH and their nearest homologs are relatively low. Moreover, the tetrapeptide motif, WRPW, which is found in all hairy and enhancer of split family members, is not present in hesr-1. Rather, a variant of this motif, YRPW, is found. Analysis of embryonic murine hesr-1 expression by in situ hybridization reveals strong expression in the somitic mesoderm, the central nervous system, the kidney, the heart, nasal epithelium, and limbs indicating a role for hesr-1 in the development of these tissues. Like the enhancer of split cDNAs in Drosophila, we show that hesr-1 expression depends critically on signaling through the notch pathway in murine embryos, suggesting that aspects of hesr-1 regulation and function might also be evolutionary conserved.

L7 ANSWER 11 OF 11 CAPLUS COPYRIGHT 2008 ACS on STN
AN 1999:553646 CAPLUS
DN 131:297930
TI Hey genes: a novel subfamily of hairy- and Enhancer of split related genes specifically expressed during mouse embryogenesis
AU Leimeister, Cornelia; Externbrink, Alexandra; Klamt, Barbara; Gessler, Manfred
CS Institute of Physiological Chemistry 1, Theodor-Boveri-Institute (Biocenter), University of Wuerzburg, Wuerzburg, D-97074, Germany
SO Mechanisms of Development (1999), 85(1,2), 173-177
CODEN: MEDVE6; ISSN: 0925-4773
PB Elsevier Science Ireland Ltd.
DT Journal
LA English
AB The authors have identified a novel subfamily of mammalian hairy/Enhancer of split (E(spl))-related basic helix-loop-helix (bHLH) genes together with a putative Drosophila homolog. While hairy/E(spl) proteins are characterized by an invariant proline residue in the basic domain and a

carboxy-terminal groucho-binding WRPW motif, our genes encode a carboxy-terminal KPYRPWG sequence and were thus designated as Hey genes (Hairy/E(spl)-related with YRPW motif). Furthermore, they bear a unique C-terminal TE(I/V)GAF motif and the characteristic proline is changed in all Hey family members to glycine. RNA in situ hybridization anal. revealed specific expression of Hey1 during development of the nervous system, the somites, the heart and the craniofacial region. Hey2 is similarly expressed in the somites whereas it shows a complementary expression in the heart, the craniofacial region and the nervous system. The diversity of expression patterns implies unique functions in neurogenesis, somitogenesis and organogenesis.

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ALL CITATIONS AVAILABLE IN THE RE FORMAT

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